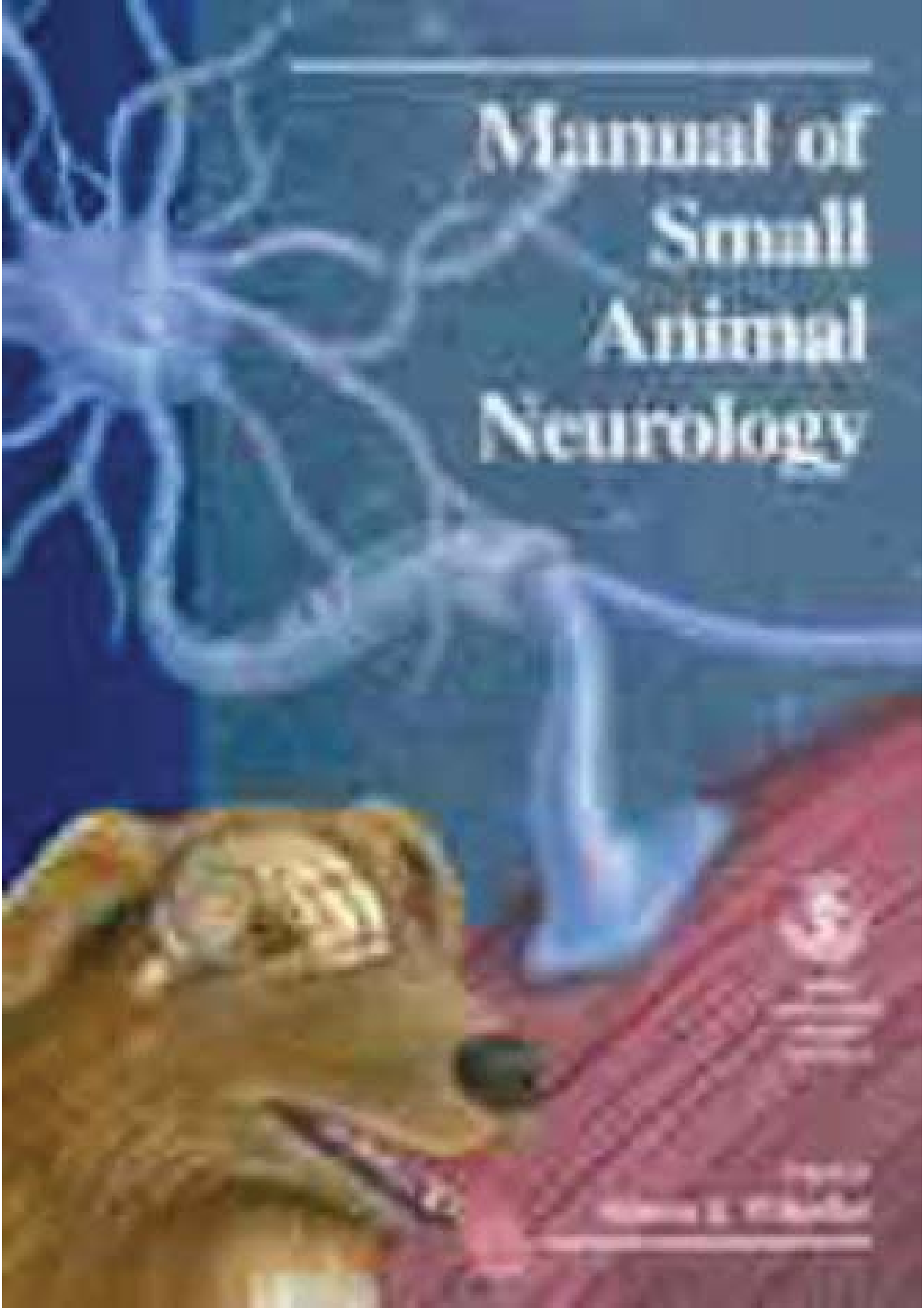
Manual of Small Animal Neurology



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BSAVA Manual of Small Animal Neurology

Second Edition

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CHAPTER ONE

Introduction

Simon J. Wheeler

The diagnosis and management of animals with neurological problems is a particularly challenging area of practice for most clinicians. The nervous system holds a particular aura, which may be due in part to the inaccessibility of its component parts for direct examination, or because of the perceived complexities of the arrangements within the system. Neurological diagnosis requires recognition of the clinical signs that result from loss of function of specific parts of the nervous system. Knowledge of the location of the affected parts allows the lesion to be localised. In essence, the nervous system is logically arranged and by adopting a systematic approach to a problem, the clinician usually can reach a satisfactory conclusion, at least in terms of making a diagnosis.

Approach to Neurological Problems

The steps in approaching a neurological problem may be summarised as follows:

- Determine the nature of the problem
- Localise the lesion
- Assess the severity and extent of the problem
- Identify the aetiology
- Evaluate treatment options
- Assess the prognosis

These steps involve making a diagnosis both by locating the lesion and identifying the disease process involved. On the basis of these findings, the clinician can decide on the best form of medical or surgical treatment, and also predict the prognosis. A rapid progression through these stages is desirable in most instances as, while many neurological conditions are amenable to treatment, prompt therapy is desirable to ensure the best possible outcome.

Determining the nature of the problem

This is the first step in the process. A full clinical examination should always precede any neurological evaluation, as it is not uncommon for disorders of other body systems to mimic neurological presentations. This is particularly so in cases where there is apparent weakness of multiple limbs, or where owners describe episodes of collapse or seizure-like activity. In the clinical examination, particular note should be made of abnormalities of the cardiovascular, respiratory and musculoskeletal systems (Table 1.1)

The neurological examination

The neurological examination provides information regarding the location and severity of the disorder. This information cannot be gained from the ancillary aids, such as radiography, but can only be obtained by a careful neurological evaluation. The performance of the neurological examination and the interpretation of the results is facilitated by the adoption of an ordered system of testing and of recording results. A typical format for recording the findings of the neurological examination is illustrated in Figure 1.1. It is not difficult to incorporate a screening neurological examination into the routine physical examination of any patient - Table 1.2.

In many instances, the complete picture in a particular case is not apparent on initial evaluation, and subsequent examinations are required to clarify the situation. There is nothing to be lost and much to be gained from making repeated neurological examinations. Also, it is important to make a complete evaluation even where the problem seems to be restricted to a single location, as other deficits may be overlooked on first examination.

Once the location of the lesion is determined, a list of differential diagnoses is drawn up. There are various methods for doing this. One ordered system is to list conditions based on the class of disorder, using the "DAMNIT (V)" mnemonic, as follows:

D	DEGENERATIVE
A	ANOMALOUS
M	METABOLIC
N	NEOPLASTIC
I	INFLAMMATORY
	INFECTIOUS
	IDIOPATHIC
	IATROGENIC
T	TRAUMATIC
(V)	VASCULAR

Use of this method will produce a list of conditions that are potential causes of the neurological problem. This list can be modified to some extent by taking the

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NEUROLOGY EXAMINATION

Date _____

Time _____

I. Subjective:

II. Objective:

A. Observation (Circle or Describe):
Mental Status: _____
Alert, depressed, stuporous, comatose

Posture: _____
Normal, head tilt, tremor, falling, paraparesis, tetraparesis

Gait: _____
Ataxia, dysmetria, circling

B. Palpation:
Muscular (tone, atrophy): _____
Skeletal: _____

C. Postural Reactions:

L	Reaction	R
	Hopping	
	Front	
	Rear	
	Proprioception	
	Front	
	Rear	
	Placing, tactile	
	Front	
	Rear	
	Placing, visual	
	Front	
	Rear	
	Wheelbarrowing	
	Extensor Post. Thrust	
	Hemiwalking	

D. Cranial Nerve Reflexes:

L	Nerve, Function Test	R
	II + VII	
	Menace	
S M L	Equality of Pupil Size	S M L
	Stim. L. Eye	
	Stim. R. Eye	
	II — Fundus	
	III, IV, VI	
	Strabismus	
	VIII + III, IV, VI	
	Nystagmus	
	Oculovestibular	
	Responses	
	V Sensation	
	V Mastication	
	VII Facial Symmetry	
	V + VII Palpebral	
	IX, X	
	Swallowing	
	XII Tongue	

E. Spinal Reflexes:

L	Reflex, segments	R
	Triceps	
	C7-12	
	Ext. Carpi Rad.	
	C7-T2	
	Flexion, fore	
	C6-T2	
	Patella	
	L4-6	
	Cranial Tibialis	
	L6-S1	
	Gastrocnemius	
	L6-S1	
	Flexion, hind	
	L6-S1	
	Perineal	
	S1-2	

F. Urinary Function:
Evidence of voluntary urination? _____
Bladder distended? _____
Ease of bladder expression? _____

G. Sensation:
Hyperesthesia _____
Superficial Pain (Panniculus reflex _____
Deep pain _____

III. Assessment:
(Lesion localization, check one)

A. Peripheral nerve _____
(Name nerve)

B. Spinal Cord
Segment 1 _____ C1-C5
Segment 2 _____ C6-T2
Segment 3 _____ T3-L3
Segment 4 _____ L4-S3

C. Brain
Brain stem _____
Central vestibular _____
Peripheral vestibular _____
Diencephalon _____
(Thalamus, hypothalamus) _____
Cerebellum _____
Cerebrum _____

D. Generalized Neuromuscular

E. Normal _____

Reason(s) for Lesion Localization
(localizing deficits):

IV. Plan:
Differential Diagnosis

Recommended Test

Figure 1.1: Form for recording findings of neurological examination

Table 1.1: Conditions that may mimic neurological disease

Type of disorder	Disorder
Bilateral orthopaedic	Osteochondritis dissecans Cranial cruciate ligament rupture Tibial crest avulsion Fractures Coxofemoral arthritis Patellar luxation
Generalised orthopaedic	Hypertrophic osteodystrophy Polyarthritis Panosteitis
Muscle disease	Infraspinatus contracture Gracilis contracture Achilles tendon rupture
Systemic	Endocrine Respiratory Cardiovascular Skeletal Other

Table 1.2: Screening tests to perform an abbreviated neurological examination

	General	Head	Eyes	Limbs
Observation	Gait Posture Mental Status	Position (±) tilt Jaw Closure Lips (±) droop Tongue mobility Temporal Muscles	Position Movements Pupils - size	Scuffing Knuckling Atrophy
Testing	Hyperaesthesia Panniculus reflex Anal relex Tail function	Jaw tone Swallowing Gagging Facial sensation Palpebral reflex	Menace response Pupillary light reflexes Oculovestibular response Fundic examination	Conscious proprioception Hopping Reflexes - Patellar Flexor

species, breed and age of the patient into account. However, it is a mistake to use such information as the sole method of reaching a diagnosis, as this will lead to mistakes. A list of breed-associated neurological conditions is given in the Appendix.

The list may also be modified by taking time-related factors into account. This is illustrated in Figure 1.2. Again, this information should not be used as the sole criteria in making the diagnosis. For example, many nervous system neoplasms show an acute or subacute onset of clinical signs, unlike the typical picture that is often described.

Clinical experience also comes into the process. It is more likely that the clinician will recognise a condition if he has seen it before!

Using this approach, a realistic list of differential diagnoses is produced, in order of likelihood. The appropriate diagnostic aids can then be selected to confirm the diagnosis.

Identifying the aetiology

Identification of the aetiology can usually be accomplished by utilising ancillary aids such as radiography, brain scanning by computed tomography (CT) or magnetic resonance imaging (MRI), CSF analysis and electrophysiological testing.

Evaluation of treatment methods

On the basis of the information gained, it is possible to decide on an appropriate course of treatment. The

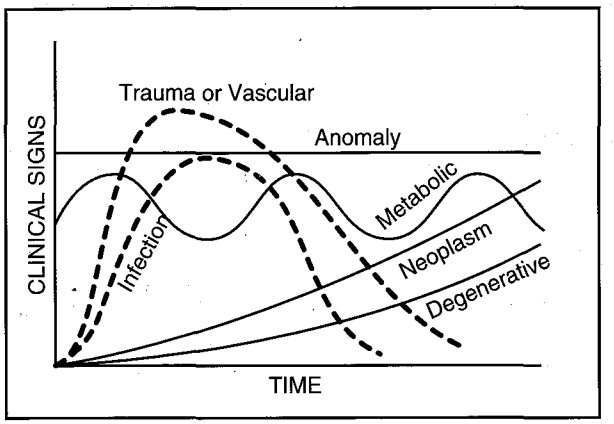

Figure 1.2: Sign-time graph of disorders affecting the nervous system. Note that this information should only be used an a guide, and not as the sole method of reaching a diagnosis.

course adopted is dependent on a number of considerations. While the aetiology of the problem is the most important, other factors may play a part, not least the wishes and expectations of the owner, the welfare of the animal, and financial constraints. Various treatment regimes may be appropriate for a particular disorder, and careful consideration of all the facets of a case is necessary to ensure that the most appropriate course is adopted.

Estimating the prognosis

Clearly, the nature of the disease has a significant influence on the prognosis, although other factors are important. The prognosis for cases with essentially similar neurological deficits is determined not only by the underlying pathological change, but also by the time course of the disorder and the duration of the deficits. For example, a dog with ataxia due to a disc protrusion carries a good prognosis for full recovery if the deficit has been present for only a few days. But if the ataxia has been present for a year, the chances of improvement are poor. Secondary problems that develop may significantly influence the outcome of an individual case, for instance, where a paraplegic dog develops a urinary tract infection. These factors must all be considered and it may be necessary to alter the prognosis as the disease progresses.

Arrangement of the "Manual of Small Animal Neurology"

This manual is arranged in three sections, with the aim of assisting the clinician with the diagnostic process and providing some information on the treatment of neurological disorders.

PART 1 discusses general principles of the neurological examination and its interpretation, with further information given in PART 2, where identifiable neurological presentations are described, and the examination, treatment and prognosis for particular conditions discussed.

The commonly employed ancillary diagnostic tests and their interpretations are dealt with in PART 1, along with a consideration of the general principles of therapeutics of nervous system diseases.

In PART 2, a problem oriented approach in used, where conditions are largely grouped and described on the basis of presenting signs.

PART 3 of the book is devoted to neurological disorders in cats and exotic species, which warrant special consideration as they may tend to become submerged in a general discussion of "small animals". These chapters are provided as additional information and should be read in conjunction with the general principles given in the preceding two sections, and also used as reference.

This manual is intended to provide a ready reference to clinicians presented with animals with neurological disorders and to give a general grounding in the subject. It is not within the scope of the book to provide detail of such topics as neuroanatomy, pathology and surgical treatment, which are covered in detail elsewhere - see Further Reading and References in each chapter. It is hoped that the information provided in this manual will enable clinicians to approach neurological problems with confidence, thus ensuring the best possible outcome for individual patients.

FURTHER READING

Delahunta A (1983) *Veterinary Neuroanatomy and Clinical Neurology*. W. B. Saunders Co., Philadelphia.

Oliver JE, Hoerlein BF and Mayhew IG, eds. (1987) *Veterinary Neurology*. W. B. Saunders Co., Philadelphia.

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CHAPTER TWO

Examination of the Head

Philippe M. Moreau and Simon J. Wheeler

INTRODUCTION

This chapter covers the examination of the nervous system relative to the brain and intracranial structures. First we describe in detail the examination of the cranial nerves, and the diseases their abnormalities may represent. Later, a system of localising brain lesions is described. See also Chapter 9 for more detail on the tests related to the eyes.

NEUROLOGICAL EXAMINATION OF THE CRANIAL NERVES

The clinical evaluation of the cranial nerves is an important part of the neurological examination of the dog or cat, especially when brain disease is suspected. The objectives of this section are to describe the examination, and the different signs of abnormal cranial nerve function. Important information concerning the integrity of the brainstem and the precise localisation of lesions is obtained from the cranial nerve examination. Each of the twelve pairs of cranial nerves originate from a specific area of the brain and innervate a specific region (Figure 2.1). The cranial nerves contain either sensory fibres (afferent fibres), motor fibres (efferent fibres) or both. Some also contain autonomic fibres. Diseases affecting cranial nerves involve either the sensory pathways, the brainstem nuclei, or the motor pathways.

Table 2.1. indicates the function and signs of dysfunction of the cranial nerves. Table 2.2. lists the respective clinical tests as well as the normal or abnormal responses for each test. As is usual practice, the cranial nerves (CN) will be referred to by number, expressed in Roman numerals.

General Considerations

In practice, evaluation of the cranial nerves is simple and quick. The cranial nerve examination does not require extensive knowledge of the anatomy of the brain, and it takes much less time to perform the examination than to read the description.

Observation

The animal is first assessed for normal posture of the head. Symmetry of the face, ears, eyes and lips is evaluated.

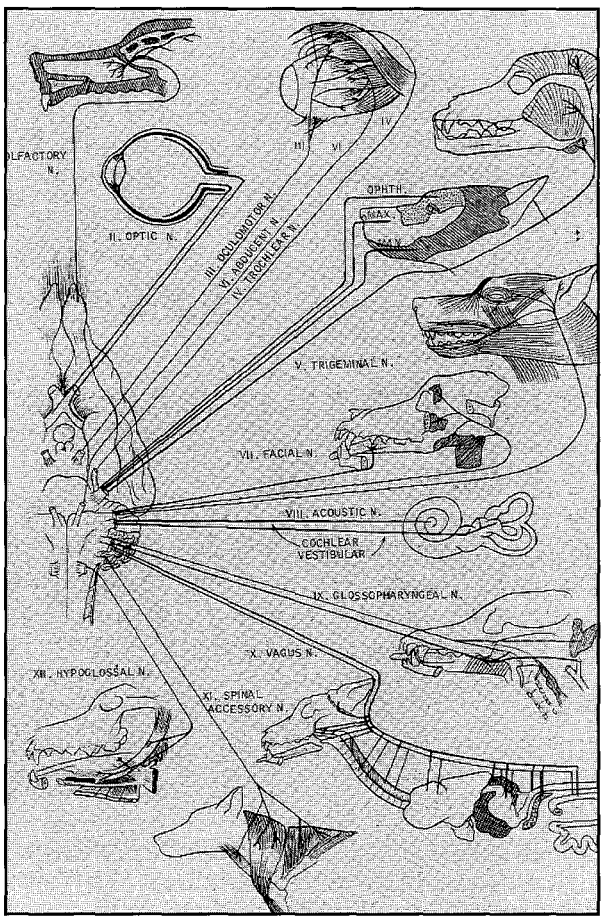

Figure 2.1: *Origin and distribution of cranial nerves in the dog. (From GREENE, C. E. and OLIVER, J. E. (1983) Neurological examination. In* Textbook of Veterinary Internal Medicine, *Vol. 1. 2nd ed. (Ed. S. J. Ettinger) W. B. Saunders Co., Philadelphia. (Reproduced by permission).*

Anomalies that can be seen with observation of the head include:

- Muscular atrophy, which may be seen in the temporal or masseter muscles, with involvement of the motor branch of CN V
- Drooping of the ears, lips or eyelids, with inability to move these structures voluntarily (CN VII)

- Abnormal position or movement of the eyes (CN III, IV, VI and/or VIII),
- Abnormal size of the pupils (CN III or sympathetic involvement)

Cranial nerve reflexes and responses

In testing cranial nerve reflexes, it is important to realise that many of the tests require two intact cranial nerves to function normally. Thus, if a reflex is absent, it may not be clear whether it is the motor or sensory arm that is abnormal. Therefore, it is necessary to test another reflex, which has some common element to the first test, in order to identify the lesion. For example, if the menace response is tested and is found to be absent, it may not be apparent whether it is the afferent component (CN II), or the efferent component (CN VII), which is defective. Testing the palpebral reflex, which is mediated by CN V (afferent) and CN VII (efferent) will further localise the lesion. If the palpebral reflex is intact, it is clear that both components of that reflex are intact, and the lesion is likely to be in the afferent portion of the menace response.

Palpebral reflex and menace response

See Chapter 9.

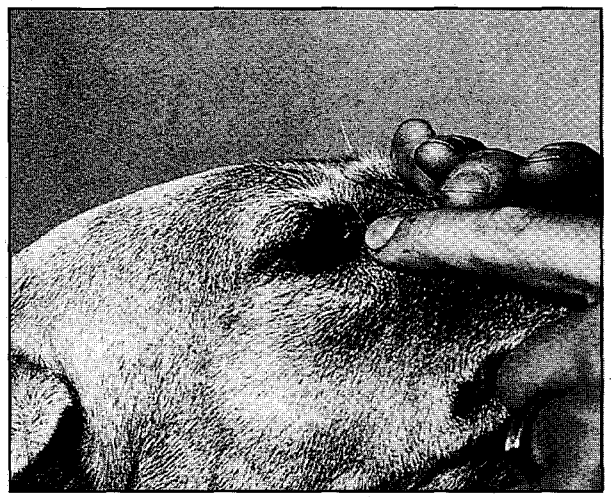

Figure 2.2: *The palpebral reflex is elicited by touching the medial canthus of the eye with the tip of a finger. If sensation is present (CN V), the animal reacts with a motor response by blinking (CN VII).*

Observation of the eyes

The palpebral fissures, controlled by the facial nerve (CN VII), should be of similar size. Eye position should be symmetrical; if not, this is termed strabismus (see page 138).

In most patients with strabismus, this indicates that the nerves controlling the extraocular muscles of the eye (CN III, IV and VI) do not function normally. The globes are then examined to determine whether or not a retracted globe is present (enophthalmia), which is often associated with an anomaly of sympathetic innervation (Horner's syndrome). At the same time, spontaneous movements of the eye (nystagmus) are looked for, indicating abnormality of the vestibular system (CN VIII).

Vision tests

See Chapter 9.

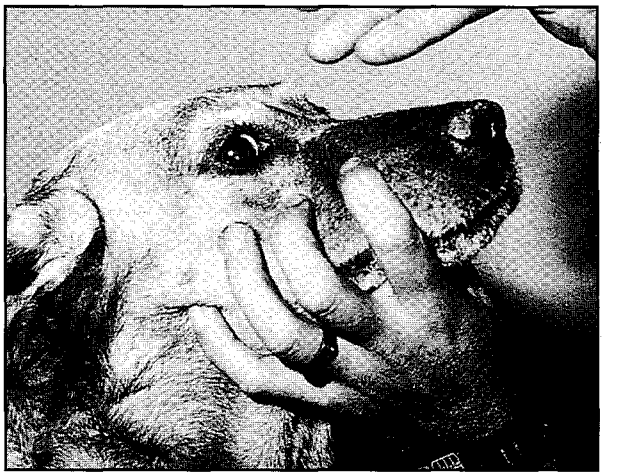

Figure 2.3: *The menace response is stimulated by abruptly approaching a hand or a finger towards the eye (simulating a blow to the eye). One must be careful not to touch the ocular structures, or to cause excessive air movement towards the eye, which would elicit the palpebral reflex. In a normal animal this test evaluates the integrity of vision (CN II) as well as the motor pathway of the eyelids, causing a blink (CN VII). Forebrain disorders can also interfere with the menace response, and cerebellar lesions can result in an absent menace responce with normal vision. Note that the menace response is absent in young animals, often up to the age to four to six weeks.*

Pupillary light reflex

See Chapter 9.

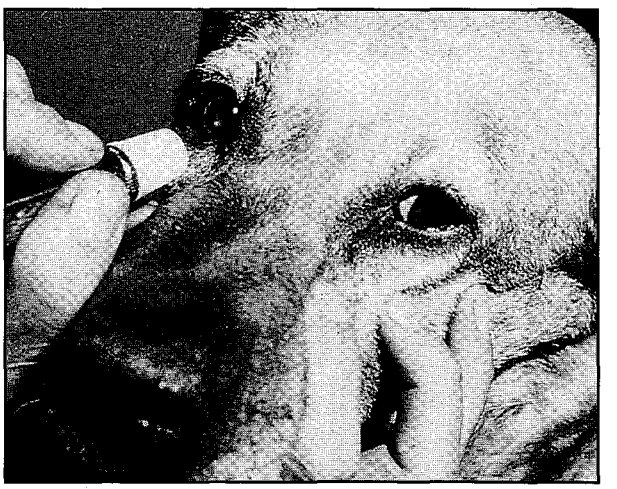

Figure 2.4: *The pupillary light relex is tested in dim light using a high intensity light source. By directing the beam towards the fundus of the eye, an immediate reflex is elicited with constriction of the pupil in the eye being examined (direct response) and also in the opposite eye (indirect or consensual response). In order for the reflex to be present, the visual pathway rostral to the lateral geniculate nucleus, and the parasympathetic fibres that innervate the smooth muscle fibres of the iris (CN III) must function.*

Table 2.1: Cranial nerve function

	Nerve	Function	Signs of dysfunction
I	Olfactory	Sensory - olfaction	Anosmia (absence of smell) Hyposmia (decreased smell)
II	Optic	Sensory - vision	Blindness (total or partial)
III	Oculomotor	Motor - external ocular muscles	Ptosis Strabismus (ventrolateral)
		Parasympathetic fibres for constriction of the pupil	Mydriasis, fixed pupil not responsive to light
IV	Trochlear	Motor - dorsal oblique muscle	Strabismus (dorsolateral)
V	Trigeminal	Sensory - skin of face	Facial hypoaesthesia or hyperaesthesia
		Motor - muscles of mastication	Dropped jaw if bilateral Atrophy of temporal muscles
VI	Abducens	Motor - lateral rectus and retractor bulbi muscles	Medial strabismus Inability to retract globe
VII	Facial	Motor - muscles of facial expression	Drooped ear, lip, inability to close eyelids
		Sensory - rostral two-thirds of tongue	Hypoaesthesia of tongue
		Parasympathetic - fibres to lacrimal gland and salivary glands (mandibular and sublingual)	Decreased tear production
VIII	Vestibulo-cochlear	Sensory - hearing	Deafness or impaired hearing
		- balance	Vestibular syndrome
IX	Glosso-pharyngeal	Sensory - pharynx, caudal tongue	Dysphagia Regurgitation
		Motor - pharynx	
X	Vagus	Sensory - larynx, pharynx, abdominal and thoracic viscera	Dysphagia Salivation disorders
		Motor - larynx, pharynx	Changed or lack of bark Regurgitation
		Parasympathetic fibres to viscera	Cardiac or gastrointestinal signs
XI	Accessory	Motor - trapezius muscle	Atrophy of neck muscles
XII	Hypoglossal	Motor - tongue	Paralysis and atrophy of tongue

Table 2.2: Clinical tests of cranial nerve function

	Nerve	Clinical Test	Normal response	Abnormal response
I	Olfactory	Smelling a non-irritant substance	Animal sniffs or licks nose	No response
II	Optic	1.Throw a piece of cotton wool in front of animal	Attention attracted	Not attracted
		2. Menace test	Eyelids close	Do not close
		3. Observe animal's movements in reduced light		Animal bumps into obstacles or wall
		4. Pupillary light reflex	Pupils constrict	Pupils do not constrict
III	Oculomotor	1. Evaluation of pupillary light reflexes	Pupils constrict	Affected eye - no response Normal eye - pupil constricts
		2. Oculocephalic reflex	Induced nystagmus in both eyes	No induced nystagmus
IV	Trochlear	Observe eye position	Normal eye position	Rotary strabismus
V	Trigeminal	1.Pinch skin of face: • Ears, lips, muzzle to evaluate mandibular and maxillary branches. • Around eyes for ophthalmic branch	Skin moves, behavioural response	No response
		2. Nasal sensation for mandibular branch	Behavioural response	No response
		3. Cornal reflex for ophthalmic branch	Blink and retraction of globe	No response
		4. Palpebral reflex	Blink	No blink
		5. Jaw tone	Resistance to jaw opening	Jaw flaccid
VI	Abducens	Corneal reflex	Globe retracts	No response
VII	Facial	1. Pinch skin 2. Corneal reflex 3. Palpebral reflex	- 1,2,3 Blink	-1,2,3 No blink, but intact sensation
		4. Schirmer tear test	4. Normal tear production	4. Reduced tear production
VIII	Vestibulo-cochlear	Auditory respose (hand clap)	Behavioural response	No response
		Oculocephalic reflex	Induced nystagmus	No induced nystagmus
IX	Glosso-phryngeal	Gag or swallowing reflex	Swallows	No swallowing
X	Vagus	Gag or swallowing reflex	Swallows	No swallowing
		Oculocardiac reflex	Cardiac rate slows	No rate reduction
XI	Accessory	Palpation of neck muscles	Normal muscle bulk	Reduced muscles
XII	Hypoglossal	Retract tongue	Animal resists	Tongue paresis

Table 2.3: Tests commonly employed to evaluate cranial nerves

Test	Technique	Nerves tested
Menace response	Simulate a blow to the eye by approaching a hand towards the face, without actually touching it	S - Optic (II) M - Facial (VII)
Pupillary light reflex	Shine light source into eye	S - Optic (II) M - Oculomotor (III)
Corneal reflex	Gently touch cornea with finger or moist cotton swab	S - Trigeminal (V) M - Abducens (VI) Facial (VII)
Palpebral reflex	Touch medial canthus of eye	S - Trigeminal (V) M - Facial (VII)
Auditory response	Clap hands behind head	S - Vestibulocochlear (VIII)
Oculocephalic reflex	Move head laterally from left to right and observe eye movements during and after movement	S - Vestibulocochlear (VIII) M - Oculomotor (III)
Pharyngeal reflex	Insert finger into back of mouth and observe swallowing	S - Glossopharyngeal (IX) M - Vagus (X)
Oculocardiac reflex	Apply digital pressure on globes by pushing on upper eyelids and measuring change in cardiac rate	S - Trigeminal (V) M - Vagus (X)

S = Sensory M = Motor

Corneal reflex

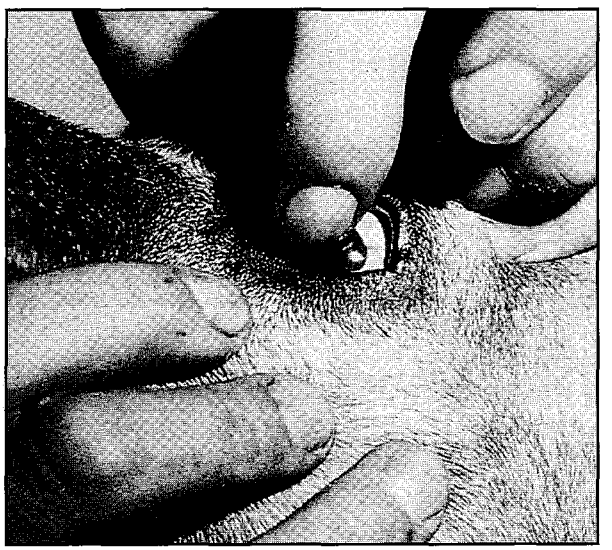

Figure 2.5: *The corneal reflex is performed by gently touching the corneal surface with a moistened cotton swab or with a finger. The animal reacts by blinking and retracting the globe. This test evaluates corneal sensitivity (ophthalmic branch of CN V), as well as the motor innervation of the eyelids (CN VII) and retractor muscles of the globe (CN VI).*

Oculocephalic reflex

Figure 2.6: *By moving the head from side to side, and then up and down, one elicits normal rhythmic lateral and vertical movements of the globe (physiological nystagmus). This tests the vestibular system (CN VIII), and the nerves controlling the position of the globe (CN III, IV, VI). At the end of each movement, the head should be stabilised and cessation of nystagmus noted. If the eyes continue to move, a positional nystagmus exists, most often associated with a lesion of the vestibulocochlear nerve (CN VIII). Aberrant eye movements unrelated to head motion are called "doll's eyes movement". This condition is usually related to severe lesions involving cranial nerves III, IV, VI and/or VIII.*

Facial sensation

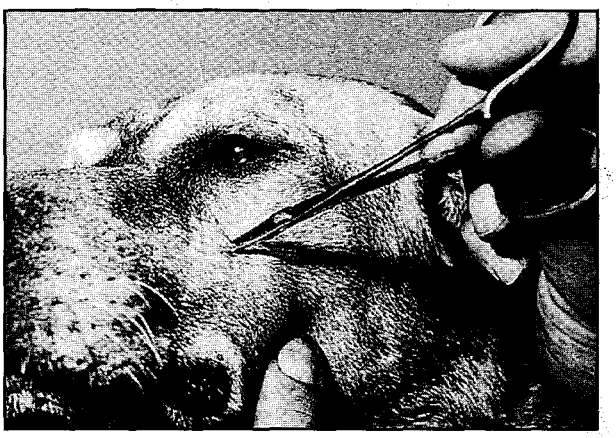

Figure 2.7 (a - left) and (b - right): *To evaluate facial sensation, areas of the face are pinched. Normally, the animal should blink in response to this stimulus, although some react more violently! In a stoical animal one may use haemostats to provide the stimuli, and observe the motor innervation of this region (CN VII). If the animal does not seem to react, one should pinch the muzzle as this area is very sensitive. Alternatively, placing a haemostat in the nares and applying pressure to the nasal septum provides an intense sensory stimulus. It is wise to cover the patient's eyes when assessing these functions. By examining successively over the various areas of the face, one evaluates the ophthalmic branches (temporal region), the maxillary branches (nasal region), and the mandibular branches (buccal region) of the trigeminal nerve (sensory) as well as motor function in the facial nerve.*

Oculocardiac reflex

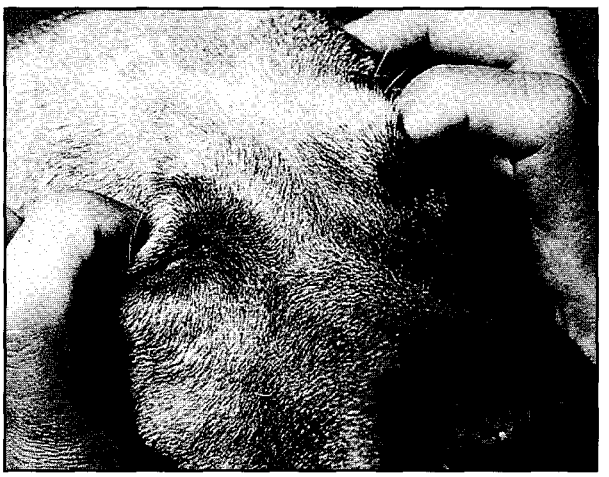

Figure 2.8: *This is performed by applying digital pressure to both globes simultaneously in order to provoke a reflex bradycardia. This test evaluates the sensory response to pressure (CN V) and the parasympathetic reflex (CN X)*

Jaw tone

By opening and closing the mouth one can evaluate jaw tone, which is indicative of the integrity of the nerves to the muscle of mastication (CN V).

Trapezius muscle

To finish the cranial nerve examination, one palpates the trapezius and brachiocephalicus muscles to verify symmetry and possible atrophy (CN XI).

Table 2.3 reviews tests commonly performed to evaluate cranial nerve function. The examination should be performed frequently, to allow the clinician to become familiar with each test. The examination should also be repeated to follow any possible change in the patient's status. A form for recording the findings of the examination is shown in Chapter 1.

Tongue

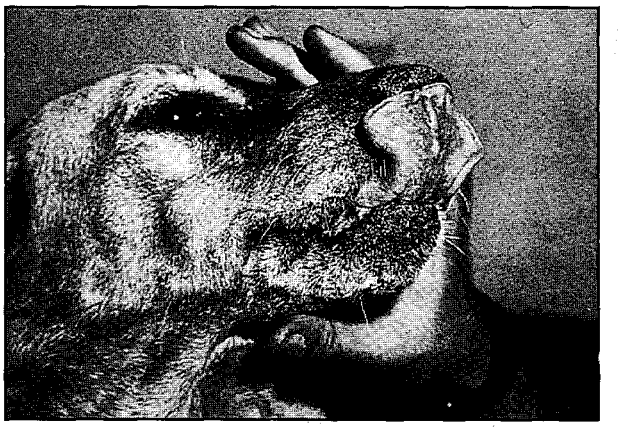

Figure 2.9: *To examine the tongue and the associated nerves (CN IX, X, XII) one first stimulates the tip of the nose (by moistening it, for example) in order to elicit a licking reflex. The symmetry of tongue movement is observed at the same time. Pulling gently on the tongue will test the muscle tone.*

THE CRANIAL NERVES

CN I - Olfactory Nerve

Function

The olfactory nerve is responsible for the conscious perception of smell.

Anatomy and clinical examination

The chemoreceptors in the nasal mucosa detect different odours and transmit the sensory information to the axons of the olfactory nerve. The nerve fibres that

dispatch this information are numerous and form an important part of the rostral brain in carnivores, especially the dog. The olfactory nucleus is situated in the olfactory bulb, which is located rostral to the olfactory peduncles in the mesencephalon.

Absence (anosmia) or decreased (hyposmia) sense of smell often is difficult to evaluate in an animal, whether it be based on the history (decreased appetite; little or no interest in food) or the neurological examination. A cotton ball soaked in alcohol, or some highly scented food may be used to stimulate a licking reaction or aversion of the head, which is a sign of odour perception. It is important to note that an animal that sniffs does not necessarily perceive odours.

Pathology and clinical signs

Lesions of the olfactory nerve are not easy to detect and are relatively rare. Chronic rhinitis with involvement of the olfactory mucosa is the most frequent cause of hyposmia. In the cat, upper respiratory infections frequently are associated with sinus congestion and subsequently a form of anorexia, which may disappear when the animal is offered odorous food (sardines etc.). Tumours of the nasal cavity also may be responsible for a lack of odour perception. Occasionally, the canine distemper virus may destroy olfactory receptor cells of the nasal mucosa as well as the neurons of the olfactory bulb and tract. Some lesions of the uncus, a part of the olfactory system, may cause hallucinations or aberrant forms of smelling, where the owner may report that the animal appears to be smelling continually something that is in fact not present.

CN II - Optic Nerve

Function

The optic nerve is responsible for sensory visual perception and the sensory component of the pupillary light reflex.

Anatomy and clinical signs

See The central visual pathway, p131, and Figure 9.9, p130.

Pathology and clinical examination

The retina and the optic disc are the only structures that can be examined directly. Because the sensory and motor fibres responsible for vision and eye movement travel through the brain to the occipital cortex and brainstem, diseases involving the brain often have repercussions on vision. The tracts and the nervous centres responsible for sight are shown in Figure 9.9, page 130.

Lesions of the optic nerve can be suspected from the history (animal bumps into furniture, etc.). The clinical tests used are discussed in Chapter 9.

Numerous diseases may affect vision (see Chapter 9 for full discussion).

Congenital problems. These include optic nerve hypoplasia, hydrocephalus, lissencephaly and lysosomal storage diseases.

Metabolic or toxic disorders. Visual deficits may be associated with metabolic or toxic disorders such as cerebral anoxia, for example, following a cardiorespiratory arrest, hypoglycaemia, thiamine deficiency (in cats), heat stroke, certain intoxications (such as by products containing lead) and osmolarity disorders (diabetic ketoacidosis).

Neoplasms. Neoplasms affecting sight include primary and secondary tumours.

CNS inflammatory diseases. These can result in a loss of vision with normal pupillary light reflexes. Other problems are often present such as ataxia, postural reflex deficits, seizures, etc., indicative of forebrain involvement.

Cranial trauma. Cranial trauma can cause contusions, haemorrhage and cerebral oedema, which in turn can trigger visual problems.

CN III - Oculomotor Nerve

Function

The oculomotor nerve controls pupillary constriction and accommodation, via its parasympathetic fibres. It is also responsible for the motor innervation of the extraocular muscles: dorsal, medial and ventral recti, the ventral oblique and the levator palpebrae.

Anatomy and clinical signs

The oculomotor nerve originates from a nucleus located in the rostral ventromedial portion of the mesencephalon.

Clinical signs associated with motor branch anomalies of CN III may include ventrolateral strabismus, reduced or absent adduction of the eye in the horizontal plane, and paralysis of the upper eyelid of the affected side (ptosis), which results in a narrowing of the palpebral fissure.

The pupils

See Differences in pupil size, p134, and Pupillary light reflex, p128, and Figure 9.11, p132.

Abnormal eye movement and position may be due to lesions of the oculomotor nerve. Eye movement is controlled by upper motor neurons from the cerebral cortex, and brainstem vestibular reflexes. It is coordinated by the synergistic and antagonistic action of the extraocular muscles innervated by CNs III, IV and VI. The centre responsible for this control is the medial longitudinal fasciculus, which is located in the centre of the brainstem between the nuclei of CN III and CN VI. A lesion in this area can induce a lack of eye movement

in response to head movements (absence of physiological nystagmus) (for more details, refer to CN VIII below). The eyes remain fixed in the orbit as the head is moved. This is sometimes called "Doll's Eye" phenomenon and often accompanies cranial trauma and cerebral haemorrhage. Such a loss of physiological vestibular nystagmus indicates the presence of extensive brainstem lesions at the level of the vestibular nuclei, the medial longitudinal fasciculus or both.

Pathology and clinical examination
Lesions of the nucleus or tracts of the oculomotor nerve produce a ventrolateral strabismus, due to a paralysis of the extraocular muscles, and ptosis of the upper eyelid caused by paralysis of the levator palpebrae muscle.

Motor function of the oculomotor nerve can be tested by slowly rotating the head in both horizontal and vertical planes, and observing associated ocular movements. By moving the patient's head from one side to the other and up and down, one should observe symmetrical eyeball movements and brief horizontal and vertical nystagmus, respectively. The fast phase should be in the direction of the head movement. This phenomenon is referred as the oculocephalic reflex. These movements depend on normal head and eye co-ordination, which is controlled by nerves innervating the eyeballs (CN III, CN IV, and CN VI) and the vestibular system. Parasympathetic function can be tested by performing the pupillary light reflexes - p128.

CN IV - Trochlear Nerve

Function
The trochlear nerve innervates the dorsal oblique muscle.

Anatomy and clinical signs
The nucleus of the trochlear nerve is small and is located in the caudal portion of the mesencephalon, caudal to the nucleus of the oculomotor nerve. Isolated anomalies are rare, difficult to diagnose and not of major interest in veterinary medicine. In cats, which have vertical narrowed pupils, a slight dorsolateral rotation of the affected eye may be observed as a result of a paralysis of the dorsal oblique muscle.

CN V - Trigeminal Nerve

Function
The trigeminal nerve has both motor and sensory portions. The motor branches innervate the muscles of mastication (temporalis, masseter, medial and lateral pterygoid, and rostral part of the digastric muscle). Its sensory branches innervate the cutaneous elements of the face including the pinnae, eyelids, cornea, oral cavity, and the mucosa of the nasal septum inside the nares.

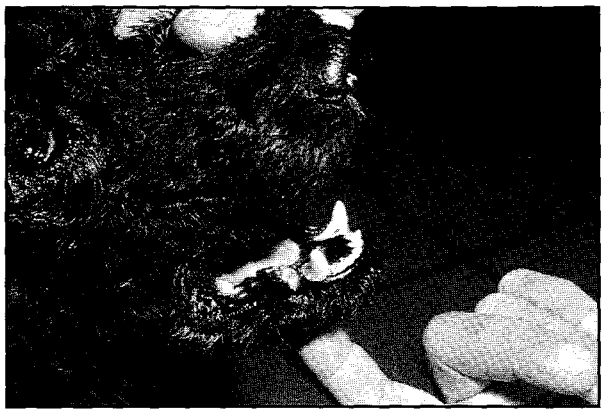

Figure 2.10: Dropped jaw due to bilateral trigeminal nerve paralysis.

Anatomy and clinical examination
The nucleus of the trigeminal nerve is not well defined anatomically, but is located in the pons in the lateral reticular formation at the level of the rostral cerebellar peduncles and dorsal to the trapezoid body. The motor axons pass through the trigeminal ganglion and the oval foramen to join the maxillary nerve tracts, and innervate the masseter, temporal, rostral digastric, pterygoid and mylohyoid muscles. Bilateral involvement produces paralysis of jaw muscles with inability to close the mouth voluntarily (Figure 2.10). Unilateral lesions can result in decreased jaw tone. These lesions are often accompanied by atrophy of the masseter and temporal muscles.

The sensory pathways of the face are distributed in three branches. The maxillary branch innervates the nasal region; the ophthalmic branch provides sensation to the ocular region and cornea; and the mandibular branch innervates the buccal area. Each branch should be tested for sensory responses (Figure 2.7, a and b). The corneal and palpebral reflexes utilise the sensory pathways of the trigeminal nerve. They also permit evaluation of the motor responses of the facial and abducent nerves by the corneal reflex, and the facial nerve by the palpebral reflex (see Tables 2.1 and 2.2). Touching the internal surface and hairs of the external ear stimulates the maxillary branch of the trigeminal nerve and normally elicits a twitching of the ear (especially in the cat) controlled by the motor pathway of the facial nerve.

Pathology
Among the diseases involving the sensory and motor function of the trigeminal nerve are infection, trauma, neoplasia and vascular disorders. Generally, other cranial nerves are also involved. A deficit in motor function is manifested by decreased muscular tone and inability to close the mouth (Figure 2.10). Bilateral trigeminal motor paralysis has been seen in rabies and idiopathic trigeminal neuritis. Most unilateral lesions do not seem to interfere with jaw function.

Certain polyneuropathies can involve the trigeminal nerve and result in atrophy of the corresponding muscles. The diagnosis can be confirmed by electromyography. It should be noted that the most frequent causes of bilateral atrophy of the muscles of mastication is masticatory muscle myositis. In these cases one must distinguish between a primary muscular disorder and a neuropathy.

CN VI - Abducens Nerve

Function

The abducent nerve innervates the lateral rectus and the retractor bulbi muscles.

Anatomy and clinical signs

The abducens nerve originates from the small abducens nucleus situated in the rostral part of the peduncular region, near the facial nerve nucleus and ventral to the floor of the fourth ventricle. Clinical examination of CN VI includes an examination of the position and movement of the eyes (oculocephalic reflex) and the corneal reflex described above. Abnormalities include medial strabismus and inability to retract the globe on the affected side. These signs are rare and often associated with disorders of other cranial nerves.

CN VII - Facial Nerve

The facial nerve is composed of motor branches that innervate the facial muscles, and sensory fibres to the palate and cranial two thirds of the tongue (providing the sense of taste).

Anatomy and clinical signs

The facial nerve nucleus is situated ventrolaterally in the peduncular region caudal to the trapezoid body, near the attachment of the cerbellar peduncles to the cerebellum. The axons cross the floor of the fourth ventricle before leaving the skull via the stylomastoid foramen, and innervating the muscles of the ears, eyelids, nose, cheeks, lips and caudal portion of the digastricus muscle.

Facial paralysis is characterised by the following:

- inability to close the eye
- paresis or paralysis of the lip commissure on the affected side
- impairment of ear movement on the affected side
- slight deviation of the nose toward the normal side as a result of unopposed nasal muscle tone
- sometimes a slight widening of the palpebral fissure, due to the lack of tone in the orbicularis oculi muscle, on the affected side.

Clinical tests which serve to evaluate various cranial nerves are also used for the facial nerve, which controls the motor response of these reflexes (menace response, corneal and palpebral reflexes, pinching the lips, stroking the hair of the external ear). Normally, if the facial nerve is affected, pinching the lips produces a painful reaction (transmitted by CN V) but the lips remain immobile due to impairment of the motor response (transmitted by CN VII).

Clinical signs depend on the location of the lesion. For example, if the lesion is external to the stylomastoid foramen, the signs described above will be present. However, if the lesion is more centrally located, as it is with areas between the medulla and the middle ear, these signs will be associated with reduced or absent lacrimation with potential keratitis sicca. A Schirmer tear test may be used to determine whether the parasympathetic fibres supplying the lacrimal gland are functional. Taste can also be evaluated using a cotton swab, by applying atropine to the surface of the tongue. The animal does not react on the affected side while he immediately responds to the bitter taste by salivating and retracting the tongue on the intact side.

Pathology and clinical examination

Idiopathic. Idiopathic causes are a common cause of isolated paralysis of the facial nerve. Several cases of facial paralysis associated with hypothyroidism have been described in dogs.

Otitis media / interna. In otitis media / interna, the facial nerve can be affected as it traverses the middle ear. In these patients, a unilateral Horner's syndrome may also be present, as the sympathetic supply passes close to the middle ear. To confirm involvement of the middle or inner ear, a thorough examination of the auditory canal (under general anaesthesia) to verify the integrity of the tympanic membrane, as well as radiography of the tympanic bulla, should be performed. Samples should be taken for culture and long term systemic antibiotic therapy should be administered.

The facial nerve may be involved in polyneuropathies (Chapter 14). The facial paralysis may be unilateral or bilateral, and the signs may or may not be isolated to a facial nerve problem.

Brainstem lesions often involve the facial nerve. In such cases, other signs of brain stem involvement (ataxia, decreased postural reactions, etc.) accompany the facial paralysis.

CN VIII - Vestibulocochlear Nerve

Function

The vestibulocochlear nerve is composed of two branches: the cochlear branch, which has a sensory role in hearing, and the vestibular nerve which is responsible for orientation of the head and body with respect to gravity.

Anatomy and clinical examination

The vestibular system consists of the end organs (utricule, saccule, and three semi-circular canals), the vestibular nerve, and four brain stem nuclei.

Together they are responsible for normal posture of the eyes, head and neck, trunk and limbs. The dorsal and ventral cochlear nuclei receive the axons that transmit acoustic information originating from the ear. Numerous nervous pathways conduct signals to the auditory centre for reflex activity as well as to the cortex for conscious perception of sound. The auditory zone of the cerebral cortex is situated in the temporal lobe.

The cochlear branch is tested by stimulating hearing with a loud, sharp sound behind the ear and observing the animal's reaction. The history often provides valuable information regarding the animal's ability to hear. Unilateral involvement is always difficult to establish clinically through the use of simple tests. Sophisticated methods, including brainstem auditory evoked potential testing (BAEP), exist to measure the electrical activity of the brainstem in response to auditory stimuli.

There are four vestibular nuclei situated on each side of the caudal part of the peduncular region, adjacent to the lateral wall of the fourth ventricle. Numerous projections leave the vestibular nuclei and travel towards the spinal cord (via the vestibulospinal tract), the brainstem (via the reticular formation) and the cerebellum (via the caudal cerebral peduncles). Through these pathways, the vestibular system co-ordinates eye, trunk, limb and head movement (see p138-140).

Anomalies affecting the vestibular branch produce characteristic signs, including ataxia, nystagmus and a head tilt. Vestibular abnormalities also may cause circling and difficulty in maintaining equilibrium and possibly hemiparesis.

Nystagmus

Two forms of nystagmus must be differentiated. One is called "jerk nystagmus" and consists of an involuntary biphasic rhythmic eye movement. There is a fast and slow phase. The fast phase is usually away from the side of the lesion, and this phase is used to characterise the nystagmus as being "right" or "left". In such disorder the slow phase is abnormal and the fast phase compensatory. The nystagmus may be present at rest or it may be induced by manipulation of the head - the latter is termed "positional nystagmus". Spontaneous nystagmus may be horizontal, rotary, or vertical. A jerk nystagmus may be observed in any lesion of the vestibular system.

Another form of nystagmus is called "pendular nystagmus". This form is less frequent and is manifested by weak ocular oscillations that have no rapid or slow components. Pendular nystagmus is seen in certain cerebellar diseases and sometimes in animals with visual problems.

Normal nystagmus can be induced by the oculocephalic reflex (Figure 2.6).

Other signs of vestibular disturbances include: head tilt toward the side of the vestibular disease (ipsilateral), falling or rolling, circling in short circles toward the side of the lesion, and ventral strabismus (ipsilateral), noted when the head is elevated. Wide excursions of the head from one side to the other may be seen with bilateral vestibular disorder.

Pathology and clinical signs

Cochlear branch. Unilateral deafness is difficult to detect clinically in domestic animals. Complete bilateral deafness generally is associated with problems of the ear itself. Given the multiple nervous pathways which transmit information to the cortex, a large margin of security exists and central lesions necessary to cause deafness must be extensive.

Congenital deafness occurs most often in white animals, notably white cats with blue eyes and Old English sheepdogs with depigmented irises. Congenital deafness also been described in other breeds, including Cocker spaniels, Dalmatians and Bull terriers.

The most common acquired causes of lesions of the cochlear branch are chronic otitis interna, cranial trauma, ototoxic medications (aminoglycoside antibiotics, for example) and degenerative disorders. Elderly patients who progressively lose their hearing may have a degeneration of the organ of Corti (spiral organ) or the chain of ossicles of the middle ear.

Vestibular Branch. Equilibrium disturbances or a vestibular syndrome may be due to either lesions of the brainstem nuclei and the central vestibular tracts (central vestibular syndrome) or lesions of the peripheral nerves (peripheral vestibular syndrome). It is important to determine the origin of the syndrome (central vs. peripheral), as a different spectrum of diseases are seen at each location, and different diagnostic tests are indicated.

Table 2.4 lists the principal clinical signs that differentiate between central and peripheral vestibular syndrome. The most reliable indicators of central vestibular disease are presence of postural reaction deficits (conscious proprioception, hopping) and nystagmus that appears or changes with alteration of head position.

Table 2.4: *Clinical signs of vestibular disease*

	Central	Peripheral
Head tilt	Yes	Yes
Asymmetrical ataxia	Yes	Yes
Nystagmus	Yes	Yes
Positional nystagmus	Yes	No
Conscious proprioceptive deficits	Yes	No
Paresis	Yes	No

Causes of peripheral vestibular disease include:
- Congenital
- Hypothyroid-related*
- Neoplasia*
- Otitis media / interna*
- Iatrogenic
- Idiopathic*
- Trauma
- Polyneuropathy

The most common are indicated by a *.

Causes of central vestibular disease include:
- Neoplasia
- Inflammatory (granulomatous meningoencephalitis, canine distemper encephalomyelitis)
- Idiopathic
- Trauma

Acute idiopathic vestibular syndrome in the cat and dog is encountered commonly in clinical practice. In the cat, this problem appears abruptly with no apparent cause (Figure 2.11). The diagnosis is made by excluding other causes. No specific treatment exists but affected cats generally improve spontaneously in two or three days, but in some cases, residual deficits remain. This condition is often erroneously diagnosed as "stroke". There is no evidence of cerebrovascular disease in these patients, which is a very rare entity in dogs and cats. A similar syndrome is seen in elderly dogs. There is no specific treatment.

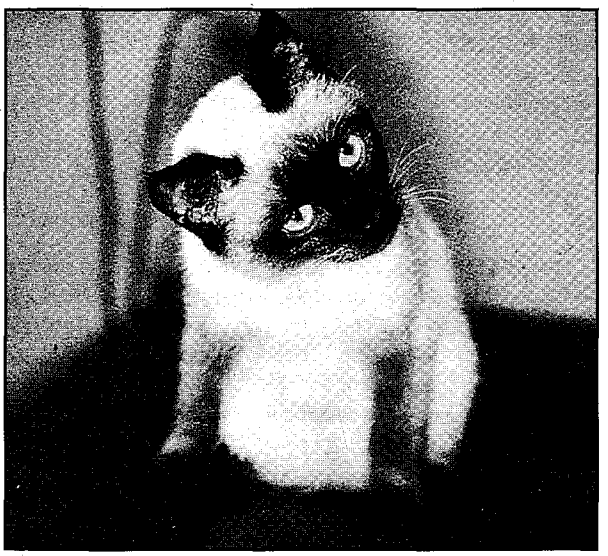

Figure 2.11: *Idiopathic vetibular disease in a young Siamese cat.*

Otitis media / interna is a common cause of peripheral vestibular syndrome. Animals with severe chronic ear infection may eventually demonstrate central signs.

Ancillary diagnostic tests to be performed depend on the location of the lesion - central or peripheral. In peripheral lesions, a thorough evaluation of the ears, including otic examination under general anaesthesia, and bulla series radiographs are required. In central disease, brain scanning and CSF analysis are indicated. Other analyses include FELV and FIP tests, toxoplasmosis titre, and BAEP.

CN IX - Glossopharyngeal Nerve

Function

The glossopharyngeal nerve innervates the muscles of the pharynx and palatine structures, in conjunction with certain fibres of the vagus nerve. For this reason, it is useful to consider the examination of these nerves simultaneously. The nerve supplies sensory innervation to the caudal third of the tongue, the pharyngeal mucosa and is responsible for taste. Also, this nerve carries parasympathetic fibres to the zygomatic and parotid salivary glands.

Anatomy and clinical examination

The glossopharyngeal, vagus and accessory nerves originate from a common nucleus, the nucleus ambiguus, in the ventrolateral zone of the medulla. The glossopharyngeal nerve emerges from the jugular foramen. The integrity of the glossopharyngeal nerve is evaluated by testing the pharyngeal reflex or "gag" reflex (Figure 2.12).

Figure 2.12: *The pharyngeal reflex is elicited by inserting a finger or a tongue depressor towards the pharynx to stimulate a swallowing or gag response.*

Pathology and clinical signs

Clinical signs seen in CN IX disorders include dysphagia and regurgitation of undigested food. Abnormalities on examination include: absence of gag reflex, reduced pharyngeal tone, and dysphagia.

Lesions affecting the glossopharyngeal nerve generally are associated with infectious diseases, trauma or tumours affecting the brainstem. Often other cranial nerves are involved and central signs can be present.

Signs of rabies and pseudorabies (Aujesky's disease) often include swallowing disorders, salivation and voice changes. These conditions should, therefore, always be included in the differential diagnosis.

Certain neuromuscular diseases are characterised by dysphagia as well as by other signs of peripheral nerve involvement, which could be due to polyneuropathies, botulism or myasthenia gravis.

CN X - Vagus Nerve

Function

Like CN IX, the vagus nerve innervates the pharynx and the larynx, and its functional examination should be combined to the glossopharyngeal nerve with regard to swallowing and the gag reflex. In addition, vocalisation and laryngeal function are controlled by the vagus nerve. The main function is to provide parasympathetic innervation to all the thoracic and abdominal viscera, except those of the pelvic region.

Anatomy and clinical examination

Sensory and motor activity of the vagus nerve is tested at the same time as that of the glossopharyngeal nerve, by the pharyngeal reflex. Parasympathetic activity is evaluated by testing the oculocardiac reflex (Figure 2.8).

Pathology and clinical signs

Vagus nerve abnormalities include: absence of the above reflexes, dysphagia, altered vocalisation, inspiratory dyspnea due to laryngeal paralysis, and megaoesophagus in bilateral vagal oesophageal paralysis.

Infectious, vascular, traumatic and neoplastic processes involving the brainstem can affect the vagus nerve. Other central signs usually are present such as motor difficulties or proprioceptive losses as well as anomalies of other cranial nerves. Altered vocalisation and laryngeal paralysis are seen in many peripheral polyneuropathies (Chapter 14).

CN XI - Accessory Nerve

Function

The accessory nerve is the motor nerve of the trapezius muscle and part of the sternocephalicus and brachiocephalicus muscles

Anatomy and clinical signs

The motor fibres of the accessory nerve originate in the ventral roots of the cervical segments (C_1-C_5) and the medulla. The fibres course towards the back of the neck and innervate the trapezius muscle, and a portion of the sternocephalicus and brachiocephalicus muscles. These muscle support the neck laterally and participate in movements of the shoulder and upper part of the thoracic limb.

Paralysis of CN XI is rare. It is accompanied by atrophy of the above mentioned muscles with a certain degree of neck deviation and dropping towards the side of the lesion.

CN XII - Hypoglossal Nerve

Function

The hypoglossal nerve is the motor nerve to the intrinsic and extrinsic muscles of the tongue.

Anatomy and clinical signs

The neurons forming the hypoglossal nerve originate in the hypoglossal nucleus in the medulla at the level of the fourth ventricle. Lesions to the hypoglossal nerve may induce: lack of retraction in response to stretch of the tongue, and lateral deviation of the tongue. In the acute phase of an unilateral hypoglossal paralysis, the deviation is on the side opposite the lesion. In chronic disorders, atrophy and fibrotic contraction result in an ipsilateral deviation of the tongue.

To evaluate the integrity of CN XII, the tongue and its motor activity are observed. All deviations and dysfunctions are noted. A licking reflex may be triggered by rubbing on the animal's nose in order to visualise the tongue and its movements.

LOCALISATION OF BRAIN LESIONS

Lesions of the brain tend to fall into clear syndromes. Accurate localisation is valuable, as certain conditions are associated with specific lesion locations. Thus, a realistic differential diagnosis can more easily be reached. The brain is divided into four functional areas for the purposes of localisation, as follows:

- Forebrain - cerebral cortex and diencephalon (thalamus and hypothalamus)
- Cerebellum
- Brainstem
- Vestibular system.

There are illustrated in Figure 2.13. In some patients, signs are seen indicating involvement of several parts of the nervous system. There are termed

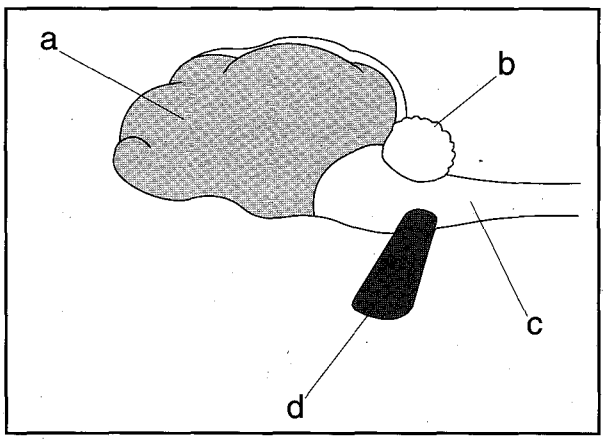

Figure 2.13: Functional areas of brain used in lesion localisation. a - Forebrain; b - cerebellum; c - brainstem; d - vestibular system.

multifocal signs. Cervical and thoracolumbar pain are frequently seen in these patients. Multifocal signs are most often caused by inflammatory disorders, with other aetiologies such as neoplasia less common.

Forebrain

Neurological signs referable to the forebrain are of two types. First, there are signs generally indicative of cerebral dysfunction. Secondly, there a signs indicating a focal lesion. Seizures, behavioural change and altered mental status are general signs. Hemiparesis, postural reaction deficits, visual and menace deficits indicate a focal lesion, and are opposite to the side of the lesion (contralateral).

Seizures are an important sign of forebrain dysfunction. Behavioural change may be manifest in many ways, including alteration of temperament, loss of house training, and failure to recognise the owner. These behavioural changes are seen quite commonly in forebrain disease, but rarely are they the only sign of forebrain involvement. Alterations in mental status, ranging from dullness and depression, through stupor to coma, are not specific for forebrain involvement, as they can also occur in brainstem lesions. Head pressing may be seen.

Many patients with forebrain signs have a relatively normal gait. However, close examination may reveal significant postural reaction deficits. These are usually asymmetrical, being worse opposite the side of the lesion. Many of these animals will circle, generally but not always towards the side of the lesion.

Visual deficits and loss of the menace response are common. The neurological examination indicates the visual deficit is caudal to the level of the lateral geniculate nucleus. Again, the deficits are contralateral to the lesion.

In some patients, more specific signs of involvement of the diencephalon are seen, such as endocrine signs, polydipsia / polyuria, and disturbances of thermoregulation.

The signs of forebrain disease are summarised in Table 2.5.

Cerebellum

The cerebellum is responsible for the "fine tuning" of movements of the body and head. Animals with lesions of the cerebellum have severe gait abnormalities. These are usually manifest as truncal ataxia, hypermetria of the limbs, and tremor. The tremor may be more pronounced when the animal is attempting a specific manoeuvre, such as eating or the visual placing test. A normal cerebellum is also required for the menace response to function; thus animals with cerebellar lesions often have absent menace responses, but normal vision. Strength is normal in animals with pure cerebellar lesions, and postural reactions are intact, although the responses may be exaggerated.

Brainstem

Lesions of the brainstem produce upper motor neuron-type locomotor signs and deficits in cranial nerve function. Mental status is also affected, because of interference with the ascending reticular activating

Table 2.5: Localising signs in brain lesions.

FOREBRAIN

GENERAL
- Seizures
- Behavioural change
- Altered mentation
- Circling

CONTRALATERAL
Deficits in:
- postural reactions
- vision
- menace response
- facial sensation

CEREBELLUM

Tremor
Hypermetria
Ataxia
Menace deficits (normal vision)

BRAINSTEM

Locomotor dysfunction:
- Hemiparesis, asymmetrical tetraparesis
- Postural reaction deficits

Cranial nerve abnormalities
Altered mental status

VESTIBULAR

Head tilt
Ataxia
Nystagmus
Positional nystagmus*
Other cranial nerve signs*
Horner's syndrome*
Altered mental status*
Postural reaction deficits*

* Features used in differentiating central and peripheral vestibular disease

system. Locomotor deficits are vary in severity, but are generally pronounced and often asymmetrical. Postural reaction deficits are generally present, and are most severe on the side of the lesion (ipsilateral). Severe lesions can result in spastic tetraplegia and complete loss of consciousness, as is seen in animals that have suffered traumatic brainstem injuries. Cranial nerve deficits are ipsilateral to the lesion, most commonly involving CNs V, VII, VIII, IX, X and XII.

Vestibular System

This is covered above under CN VIII - Vestibulocochlear nerve.

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CHAPTER THREE

Neurological Examination of the Limbs and Body

Ian R. Griffiths

PRINCIPLES UNDERLYING THE NEUROLOGICAL EXAMINATION

Introduction

Before describing the practical details of the performance and interpretation of the neurological examinations, it is essential to understand what the clinician is attempting to achieve. The obvious questions that ideally should be answered are:

- (a) where is the problem?
- (b) what is causing it?
- (c) how severe is the damage?
- (d) what is the prognosis?

Points (a) and (c) usually can be determined from the clinical examination, while (b) often requires further information such as history and ancillary tests.

Upper and Lower Motor Neurons and Sensory Fibres in Relation to Limbs

Upper motor neuron

The upper motor neuron (UMN) can be regarded as a neuron originating in a motor centre in the brain, and travelling down the spinal cord to synapse, via interneurons, with the lower motor neuron (Figure 3.1).

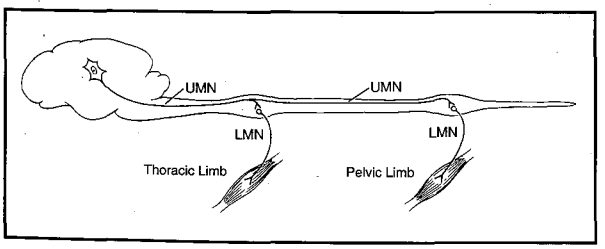

Figure 3.1: *Diagramatic representation of upper (UMN) and lower (LMN) motor neurons supplying the limbs. The UMN is shown as a single neuronal pathway and no interneurones are included.*

Lower motor neuron

The lower motor neuron (LMN) has its cell body located in the ventral horn of the grey matter, with the axon running in the ventral nerve root and peripheral nerve to supply the appropriate muscle.

The motor unit is the basic functional unit comprising the LMN and muscle fibres that it supplies. Limb muscles are invariably innervated by fibres originating in more than one spinal segment.

The LMN is the final common pathway for motor activity, whether voluntary or reflex. Most of our clinical tests examine local limb reflexes, which require afferent fibres and perhaps interneurons to complete the reflex arc. The type of peripheral receptor and afferent fibre will vary according to the nature of the reflex and the stimulus used to initiate it (e.g. noxious stimuli or muscle stretch) (Figures 3.1 & 3.2).

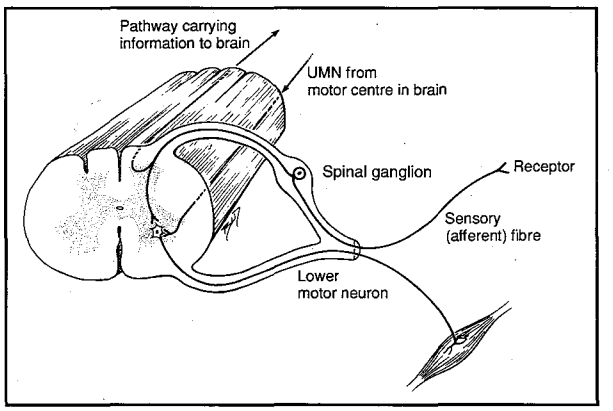

Figure 3.2: *Representation of a simple reflex arc that serves a clinically-testable reflex. Damage to either the LMN or the sensory fibre or both will interrupt the reflex. This feature is used in distinguishing lesions in these neurones from those in the UMN or in sensory pathways in the spinal cord.*

The effect of lesions on these pathways

These are best appreciated by reference to Figure 3.2 and Table 3.1. Motor problems (e.g. weakness or paralysis in limbs) should be classified as either UMN or LMN in type. The major clinical differentiation is by the effect on muscle tone, local reflexes and muscle bulk. Variation in the severity of damage can cause gradation of signs. In acute LMN lesions, the depression or loss of tone and reflexes occurs early, while atrophy takes up to three weeks to become evident. In more chronic LMN lesions, atrophy can be obvious by the time the animal is first presented.

Table 3.2 compares the effects of LMN and afferent fibre (sensory) lesions. Some effects such as reflex loss may be common to both. In many peripheral nerve diseases or injuries, both sensory and motor fibres are damaged, causing a combination of the signs.

Table 3.1: Differentiation of upper and lower motor neuron lesions

	LMN		UMN	
	Complete	**Partial**	**Complete**	**Partial**
Motor function	Paralysis	Paresis	Paralysis	Paresis
Muscle tone	Absent	Decreased	Present but may be altered in character	
Local reflexes	Absent	Depressed	Present but may be altered in character	
Muscle atrophy	Severe*	Less severe	Minimal	Minimal

* The atrophy will take some time (2-3 weeks or more) to become clinically obvious

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Table 3.2: Comparison and differentiation of lower motor neuron and sensory neuron lesions

	LMN	**Sensory**
Motor function	Paresis/paralysis	Present, but may be ataxic
Sensory function	Normal	Deficit*
Local reflexes	Absent/depressed	Absent/depressed*
Muscle tone	Absent/reduced	Probably reduced*
Muscle atrophy	Severe	Mild

*The exact sensory deficit and the involvement of reflexes and tone will depend on type(s) of sensory fibres affected, e.g. if large diameter primary afferents from spindles are involved, the patellar reflex and muscle tone would be affected.

INITIAL NON-NEUROLOGICAL EXAMINATION

It is assumed that a general physical examination is performed. In many instances this is best done before the neural examination, because systemic diseases can affect these tests even if the nervous system does not appear directly involved (Chapter 1). For example, a dog with severe cachexia or hypovolaemic shock will not react to neurological testing in the same way as one in which these features are absent. There are also certain non-neurological conditions which, on superficial examination, may be confused with nervous disease. Following acute trauma, pelvic fractures or bilateral limb fractures can produce a clinical picture somewhat resembling paraplegia related to a spinal injury. Acute bilateral cranial cruciate rupture can also lead to confusion, and in all instances the femoral pulses should be checked. The moral, therefore, is to make sure there are no orthopaedic or vascular problems that could be misdiagnosed.

NEUROLOGICAL EXAMINATION

General Approach

Disturbances in gait are one of the most common reasons for neurological investigation, usually presenting as a motor problem (paresis or paralysis), incoordination (ataxia), or a combination of these. The first stage of the physical examination usually involves ascertaining the animal's ability to make co-ordinated movements. Often, this can be achieved by watching the animal walk or attempt to walk. If this is not possible, the patient can be supported as necessary so that any movement, however weak, can be noted. At the end of this stage it should be possible to determine which limbs are involved, if there is lateralisation of signs and if weakness and/or ataxia is present. (See Wheeler & Sharp 1994 for more details of test performance).

Ataxia and weakness

It can sometimes be difficult to distinguish the effects of weakness and ataxia on the gait. Ataxia caused by spinal or peripheral lesions commonly produces a swaying, swaggering gait, with occasional hypermetria and catching of limbs. It gives the impression of misapplied power, and is best observed at a slow steady pace rather than a faster walk. Pure motor signs can be seen in diseases such as myasthenia gravis and motor polyneuropathies. In such instances, the animal has a stiff, stilted gait, takes shorter strides, often has a degree of postural tremor, and usually collapses or rests after a short distance. The movements, however, remain co-ordinated. In many conditions both ataxia and weakness are present.

Acute injuries

Following acute trauma where a spinal injury is suspected, the animal should not be encouraged to move until the nature of the damage is known. Some indication of motor function may be gained by watching spontaneous attempts to move, but efforts to support the animal and encourage it to move could lead to further spinal damage.

Motor function

Motor function can be assessed in the tail, but it is important to ensure that tail wagging is spontaneous. Reflex wagging can occur after spinal cord injuries if the dog is handled around the hind end. Axial weakness may be indicated by the inability to hold up the head and support the trunk, resulting in a "floppy dog".

More specific examination of motor function can then be made. By lifting a contralateral limb the strength of the ipsilateral extensor muscles can be assessed. For example, weakness in the triceps would lead to dropping of the elbow. Some of the flexor groups can be tested for their ability to move the limb against gravity. For example, in attempting a visual placing test, the elbow joint is flexed to lift the limb onto the table surface. The wheelbarrow test (where the weight is taken on both thoracic limbs during walking while the rear end is supported), and the hopping test (where the weight is taken on a single thoracic limb during walking) are very useful to unmask latent paresis in the thoracic limbs. Weakness is usually demonstrated by the dog knuckling on that limb, the head and neck dropping, and the animal tending to somersault. The weakness can be the result of UMN, LMN, muscle and sometimes orthopaedic problems.

Co-ordination

Co-ordination can be examined further by turning the animal in circles, especially on a slippery surface, and by walking up or particularly down steps. Tests such as hemistepping are also useful. Co-ordination of gait and movements requires intact unconscious proprioceptive information from the limbs as well as other inputs from eyes, vestibular system, etc. These inputs and the resultant adjustment of motor function are mediated via the cerebellum.

Conscious proprioception

Other tests are designed to look at conscious proprioception, that is, the conscious awareness of limb position and movement, which depends on connections to the somatosensory cortex. These tests are paw position sense, "reflex stepping", and sway response. Conscious proprioceptive deficits are seen in many neurological diseases, and are sensitive indicators of nervous involvement. The deficits are seen caudal to a lesion, but note that they may be more severe in the pelvic limbs, even in intracranial lesions.

Paw position is tested by turning the foot so that the dorsum of the paw is in contact with the ground. A normal animal will return the foot to a normal position immediately, whereas one with a proprioceptive deficit may leave the foot in the inverted position.

The "reflex step" is tested by placing a sheet of paper beneath the foot and pulling it sideways; the normal animal rapidly returning the foot to a standing position.

The weight of the animal's body should be supported during these tests and each limb assessed individually.

The sway response is tested by pushing the trunk sideways, and observing the animal regain a normal upright position. Animals with neurological deficits may find this difficult or even fall over.

The conscious proprioceptive tests require a motor response, and it is therefore pointless to perform them if the animal has insufficient motor function to return the limb to the correct position.

Examination of Individual Limbs

A general visual assessment may reveal worn nails or scuffed paws, suggesting dragging or knuckling of the limb. Atrophy is detected by vision and palpation. Determine if the atrophy is generalised or selective, taking into account the duration of the disease and the general physical state of the patient. If a unilateral condition is present, compare side to side.

Muscle tone and local limb reflexes are assessed with the animal lying relaxed on its side. In most instances sufficient relaxation can be achieved, but in tense animals, muscle tone and the patellar reflex can be markedly affected.

Muscle tone

This is the resistance to passive stretch and depends chiefly on the stretch reflex. It is assessed by flexing or extending a joint to stretch an appropriate muscle, for example, flexing the stifle joint will stretch the quadriceps muscle. The resistance to stretch is graded subjectively by the clinician as being within normal range, increased or decreased. Increased tone can be subdivided into: a) spasticity where the tone increases after an initial period of stretch (the free interval) during which resistance is normal; b) rigidity where there is no initial free interval. This differentiation of spasticity and rigidity is perhaps not so important in veterinary neurology as in human medicine. In these states of hypertonia, the resistance will usually decrease after initially increasing. This can be a gradual lessening of resistance or involve a sudden collapse of the limb - the "clasp knife" phenomenon.

Spasticity is usually associated with UMN lesions, either in the spinal cord or brain stem. Rigidity may be seen in certain muscle diseases such as Cushing's

disease myopathy, or the polyneuromyositis of neosporosis, and in the interneuronal destruction caused by ischaemia of the intermediate grey matter.

Hypotonia is seen in LMN lesions or in sensory neuropathies affecting the larger diameter afferent fibres. It should be remembered that in many neurological disorders, muscle tone is within normal limits.

Patellar reflex

This is an example of a phasic stretch reflex initiated by tapping the straight patellar ligament, thus causing a synchronised activation of the muscle spindles. The response is a twitch-like muscle contraction of the quadriceps muscle, causing the distal limb to move forward before relaxing. At the end of this contraction/relaxation there are imperceptible oscillations as the movement is damped down. The afferent and efferent pathways are in the femoral nerve, and the central connections lie in segments L_4, L_5 and L_6. In most relaxed dogs the reflex is obtained easily, but is more difficult in pups, cats and tense dogs. The test should be performed in the uppermost limb, with the stifle slightly flexed to provide some stretch to the muscle. If there is some doubt as to whether a response is present or not, perhaps because the dog is tense, then the lower limb should be tested as this often is more relaxed. As this limb is against the surface of the table it is difficult to observe the character of the response, but its presence or absence can be verified. In young pups, the reflex may also be tested by suspending the pup under the thoracic limbs and allowing the pelvic limbs to dangle.

In UMN lesions the reflex usually is present but may be altered in character. In severe, acute spinal injuries, the response may be decreased for several days following the damage. Typically, in UMN lesions, the response may be exaggerated with a tendency to oscillate at the end of the relaxation phase, that is, clonus. Less commonly, clonus may be observed when muscle tone is increased. Under these circumstances there is a rhythmic series of contractions, mainly during the relaxation phase of the response.

The reflex is depressed or absent in LMN lesions, or those involving the larger diameter sensory fibres. As femoral nerve lesions are relatively uncommon, this situation is usually seen in polyneuropathies or in diseases or injuries affecting the lumbar enlargement and appropriate nerve roots. The reflex may also be depressed or absent in some cases of degenerative myelopathy (chronic degenerative radiculomyelopathy - CDRM), where there is involvement of larger diameter afferent fibres in the dorsal nerve roots

In some sciatic nerve LMN lesions, the patellar reflex, while present, may oscillate excessively due to the paralysis of the antagonistic hamstring muscles. This is sometimes termed "pseudo-hyper-reflexia", which is different from true hyper-reflexia, as there are LMN features in the muscles innervated by the sciatic nerve.

Pedal reflex

This is also known as the flexor or withdrawal reflex, and involves the withdrawal of the limb from a painful stimulus. The receptors are the free nerve endings in the skin, sensitive to noxious stimuli, and the afferent pathways are in small myelinated fibres. The motor output is to all the flexor muscle groups in the limb, and therefore involves several peripheral nerves and spinal cord segments. The stifle and hock flexors are innervated chiefly from segments L_6, L_7 and S_1, via branches of the sciatic nerve. The hip flexors have more widespread innervation, mainly from lumbar segments and the femoral nerves.

To test the reflex, the inter-digital skin is squeezed between the index finger and thumb, at the same time putting slight longitudinal tension on the limb, so that it must be withdrawn against such tension. (In some patients it may be necessary to place forceps across the animal's nail.) This allows some assessment of the strength of the flexor groups. It is important to observe that all the flexor groups are functional, as it is not unusual to uncover selective weakness in muscles, most commonly in the hock flexors.

In UMN lesions, the reflex should be present, and it is common to find a prolonged contraction continuing after the cessation of the noxious stimulus.

In addition to the withdrawal reflex, other reflex activities may be noted: a) the crossed extensor reflex in which there is extension of the contralateral limb as the ipsilateral limb is flexed, b) reflex tail wagging, which also occurs while the toes are being pinched.

In LMN lesions, all or parts of the reflex may be lost depending on the location of the damage in the cord or peripheral nerves.

Anal reflex

Although not a limb reflex, this function should be assessed as it gives information regarding the integrity of the sacral segments and nerve roots, and is obviously important for faecal continence. It should be observed if the anus is closed or gaping, and the perianal skin should be flicked. This will result in a wink-like contraction of the sphincter, usually accompanied by a downward movement of the tail head and an upward movement of the vulva. Finally, and if necessary, anal tone can be assessed during a rectal examination. In LMN lesions involving the sacral segments or cauda equina, the reflex may be lost and the anus may be flaccid.

Local reflexes in the thoracic limbs

Tendon reflexes - biceps and triceps tendon jerks - can be elicited but are inconsistent in normal dogs. It is probably not worthwhile performing these tests. The pedal reflex is obtained in the same manner as for the pelvic limbs, noting if there is flexion of shoulder, elbow and carpal joints.

Grading system for neurological tests

Many clinicians use a standard format for recording the results of various neurological tests, as follows:

Grade	Reflex or Reponse
0	Absent
+1	Reduced, but intact
+2	Normal
+3	Increased
+4	Clonus

Other Functions to be Assessed

Panniculus Reflex

This is the well known twitch of the skin over an animal's back in response to a stimulus over that area. The effector organ is the cutaneous trunci muscle (formerly "panniculus carnosus muscle"), innervated by the lateral thoracic nerve, which originates from the caudal brachial plexus and receives its fibres from segments C_8 and T_1. The receptive field is a saddle-shaped area over the chest wall and flank extending to, or just caudal to, the iliac crest. Although there is an output for the reflex at C_8/T_1, the afferent side is organised on a dermatomal basis with inputs at many segmental levels from about T_3 to L_1, representing the area of skin over the trunk. Interneurons, probably located in the ventrolateral white matter, connect the afferent and efferent pathways (Figure 3.3).

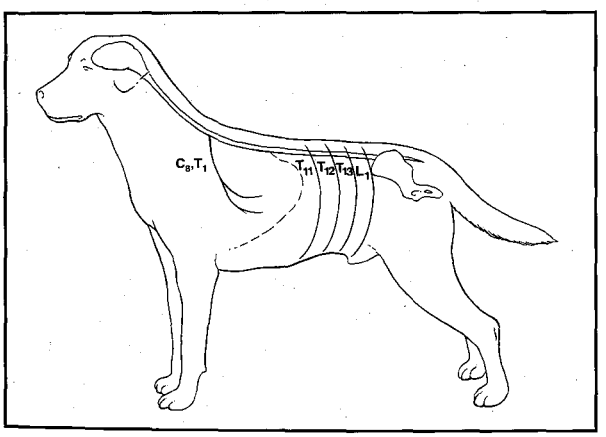

Figure 3.3: Outline of the panniculus reflex to show the single outflow at C_8 -T_1 and the caudal borders of dermatomes T_{11}-L_1. These have been identified by matching the level of "cut off" of the reflex to underlying cord damage as determined at post-mortem. If, for example, a lesion was present at T_{12} then T_{11} would be the intact segment immediately cranial to this and the panniculus "cut-off" would be just behind the last rib as indicated.

Using a light pin prick or forceps pinch, the skin is stimulated about 2-3 cm lateral to the mid-line, starting at the level of the iliac crest. The response should be a twitch of the skin, which usually is stronger ipsilaterally, but should be present bilaterally. This twitch should be distinguished from the lordotic movement of the back that sometimes occurs in response to the prick, which represents a withdrawal reflex from a painful stimulus. If the panniculus reflex is not present at the level of the iliac crest, the stimulation should proceed cranially until a line is found above which the twitch occurs. This level represents the caudal border of the last intact dermatome. Sometimes, reflex tail wagging is noted as the skin is stimulated behind this level.

Damage to the outflow can also occur either with cord lesions at C_8/T_1 or, more commonly, avulsion of these nerve roots (brachial plexus root avulsion). In such circumstances, the skin twitch is absent over the whole of the receptive area, ipsilaterally in the case of root avulsions and perhaps bilaterally with cord damage. With nerve root avulsions a strong consensual response usually is evident.

The panniculus reflex can, therefore, often be used to locate the site of damage either to the spinal cord, or nerve roots / brachial plexus. In thoracolumbar cord lesions the cut-off represents the caudal border of the last intact dermatome cranial to the lesion, indicating that the cranial extent of the damage is the next caudal segment. The caudal levels of dermatomes can be determined by various experimental or clinical methods, and show some variation according to the technique used and the sensory modality tested. Figure 3.3 illustrates the caudal borders of dermatomes around the thoracolumbar area as determined by the site of "cut off" of the panniculus reflex correlated with the location of the underlying cord lesion. (This map does not necessarily correspond to one obtained using other methods, for example, electrophysiological recordings from nerve roots.)

If an animal has lost pain sensation behind a cord lesion it is usual to find the panniculus "cut off" and level of pain sensory loss correspond, but the two functions are not inter-related and it is common to find animals with intact pain sensation and interruption of the panniculus reflex. The panniculus reflex will only show abnormalities if the lesion is within the appropriate anatomical area, i.e. C_8-L_1. Therefore, cervical cord, lower lumbar and sacral problems have an intact reflex. In certain circumstances lesions can also occur between C_8 and L_1 and leave the panniculus reflex intact. Very mild damage is often not associated with panniculus loss, and some diseases may spare the interneurons concerned with the reflex. For example, in CDRM, degeneration occurs in the thoracic and lumbar white matter, but the panniculus reflex invariably is intact. In traumatic or compressive myelopathies between C_8 and L_1 it would be highly unusual for the panniculus not to be affected where there is a lesion sufficient to cause more than moderate paraparesis.

Assessment of pain sensation

The appreciation of pain is obviously subjective, and whether an animal is feeling pain must be inferred by its response to noxious stimuli. The quality and inten-

sity of pain can be modified at a number of levels in the CNS. As can be commonly observed, individuals respond differently to apparently identical stimuli. In a single animal some comparisons can be made between thoracic and pelvic limbs, or left and right sides.

Assessment of pain sensation requires a noxious stimulus and an evaluation of the animal's response. In regard to limbs, the interdigital skin can be pinched between finger and thumb. A more consistent stimulus can be provided by gripping across the nail with forceps. It is advisable to stimulate both medial and lateral sides of the foot. Forceps pressure can also be used on the tail. Use of pin prick is more difficult to interpret. Failure to respond should not be taken as evidence of absent or diminished pain sensation.

In general terms, one is looking for a response from the "front end" of the animal. This may involve yelping, snarling, attempting to bite, turning to look at the stimulated site, licking the lips, or even a "hurt expression" of the eyes. The response will vary from dog to dog. A movement (e.g. a withdrawal) of the stimulated area from the noxious stimulus is the result of a local reflex, and should not be taken as evidence of pain sensation. This is a common mistake made in assessing animals with spinal lesions, and is of great importance, because of the difference in prognosis between animals with and without pain sensation.

Over the limbs, loss of pain sensation may occur as the result of a cord / nerve root problem or peripheral nerve lesions. Cord or root damage will cause loss in a dermatomal pattern, corresponding to the caudal border of the last intact dermatome.

Bladder function

Bladder control and continence are important and may be impaired in spinal cord or cauda equina lesions. The local parasympathetic innervation of the bladder is from the sacral segments via the pelvic nerves, while the urethral sphincter is also innervated from these segments via the pudendal (pudic) nerve. Besides local segmental innervation of the bladder, long supra-spinal reflexes to centres in the reticular formation are necessary for micturition. Spinal cord injury rostral to the sacral segments (the equivalent of an UMN lesion) may damage these connections, resulting in inability to urinate. The damage, which must be bilateral, usually results in urinary retention and overflow - a large volume distended bladder with dribbling of urine. Injuries to the sacral segments, sacral nerve roots or pelvic nerves (LMN) can either cause a similar situation or a small volume bladder also with incontinence.

Following damage rostral to the sacral cord (UMN bladder) recovery may occur. Alternatively, an automatic bladder, emptying by reflex to raised intracystic pressure, may develop. Full recovery following LMN lesions can occur but is less likely.

The involvement of the bladder following cord injury and disease depends markedly on the type and severity of the lesion, and in many instances function is unaffected. In many types of polyneuropathy, bladder control is spared.

Assessment of bladder function is discussed in Chapter 12.

Sympathetic function

The cell bodies of the preganglionic fibres lie in the thoracic and rostral lumbar segments. After synapsing in sympathetic ganglia, many post-ganglionic fibres supply peripheral blood vessels. Structures in the head receive their sympathetic innervation from the first few thoracic segments via the vagosympathetic trunk. Central sympathetic fibres descend from various brain stem nuclei to synapse with the preganglionic fibres, and it is these descending fibres which may be damaged in cord disease.

Two major effects may be noted:

a. Skin hyperthermia due to loss of vascular tone and increased skin blood flow. In cervical lesions this can affect the head, body and limbs, whereas in thoracic lesions the body and limbs caudal to the lesion are involved.
b. Horner's syndrome following cervical cord, T_1 nerve root, vagosympathetic trunk or post-ganglionic (usually middle ear) lesions. A complete Horner's syndrome consists of myosis (the pupil will respond to changes in light intensity), ptosis of the upper lid, protrusion of the membrana nictitans and slight enophthalmos. In T_1 nerve root lesions, usually caused by brachial plexus avulsion, a partial Horner's syndrome with myosis is the usual evidence of sympathetic damage (See Chapters 2 and 9).

In other peripheral nerve injuries the affected limb may also appear warmer due to sympathetic damage. In most instances, skin hyperthermia, due to either central or peripheral lesions, is seen only in the acute stages and later resolves. Also, in many cases of cord disease or injury, the sympathetic system remains intact.

Schiff-Sherrington phenomenon

Following damage (usually severe) to the thoracic spinal cord the thoracic limbs may become rigidly extended, with marked increase in extensor tone. Even when the digits are pinched, the withdrawal reflex may be sluggish because of the extension. Voluntary movement is still present, although it is markedly reduced by hypertonia. This extension of the limbs is known as the Schiff-Sherrington phenomenon, and is associated with either direct damage to the thoracic cord or extension of damage from a more caudal level into the thoracic segments, for example, in the ascending syndrome following thoracolumbar disc protrusions. The Schiff-Sherrington phenomenon is usually an indication of poor prognosis.

Paradoxical respiration

During normal inspiration, the rib cage is tensed and rotated outward and forward by the action of intercostal and other muscle groups, while the diaphragm flattens. These procedures decrease endothoracic pressure and cause the inward movement of air. If all or the majority of the chest wall is paralysed, respiration is achieved by diaphragmatic movement while the thoracic wall moves passively with changes in thoracic pressure. The chest wall therefore moves inward during inspiration. Paradoxical respiration is seen with cranial thoracic cord lesions, which sever the descending pathways to intercostal motor neurons or extensively damage the motor neurons themselves. It may well be concurrent with the Schiff-Sherrington phenomenon.

Procedure for Neurological Examination of Spinal Cord and Peripheral Nerves

(Following history and physical examinations)

1. Watch the animal walk and stand (support if necessary)
2. More specific tests of weakness (hopping, wheelbarrow, etc.)
3. Conscious proprioceptive tests (paw position, sway, "reflex stepping")

(Great care in acute spinal injuries)

4. Lie animal on side for local pelvic limb examination
   a. Muscle tone
   b. Patellar reflex
   c. Pedal reflex - at the same time check conscious pain sensation
   d. Muscle atrophy
5. Thoracic limb examination
   a. Muscle tone
   b. Pedal reflex - check conscious pain sensation
   c. Atrophy
6. Panniculus reflex
7. Skin temperatures (compare left to right - thoracic limb to pelvic limb)
8. Horner's syndrome (and cranial nerve examination)
9. Other signs e.g. Schiff-Sherrington, neck pain, paradoxical respiration.
10. Bladder function

Localisation of Cord and Nerve Lesions Causing Limb Signs

After obtaining the history and watching the animal walk (if appropriate), some judgement on localisation can be formed on the basis of probability.

Motor signs (weakness/paralysis) and/or ataxia in thoracic and pelvic limbs

Lesions in cervical spinal cord or brain, or a diffuse peripheral nerve problem (polyneuropathy)

Motor signs more pronounced in thoracic limbs than in pelvic limbs

Probably cervical cord problem or, less likely, a bilateral peripheral problem in thoracic limbs.

Motor signs and/or ataxia in pelvic limbs with normal thoracic limb function

Spinal cord lesions caudal to brachial outflow, or bilateral peripheral problem in pelvic limbs.

Monoparesis/plegia

Most probably peripheral nerve problem in that limb.

(Brain lesions will not be described further here as they are discussed in Chapters 2 and 8.)

Assuming that a motor problem is present, the next stage is to ascertain whether it is UMN or LMN, or a combined UMN/LMN deficit. This is based on the presence or absence of local limb reflexes, muscle tone and atrophy, as discussed above and in Table 3.1. This categorisation of the motor problem allows further definition of the lesion, as indicated in Table 3.3 and Figure 3.4. Other tests or signs may then be used for more precise localisation, as indicated in Table 3.4.

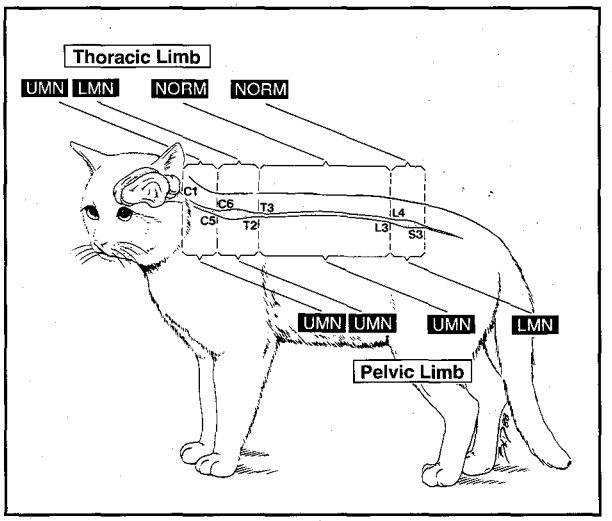

Figure 3.4: *To be used in conjunction with Table 3.3. The diagram of the spinal cord segments indicates how damage at a particular area can affect motor function in thoracic or pelvic limbs in terms of causing an upper or a lower motor neuron type of dysfunction. (From Wheeler S.J. (1989) Spinal Tumours in Cats. In* Veterinary Annual ***29****, 270-277, reproduced by permission).*

Table 3.3: Motor problems and lesion location

Type of Motor Problem	Probable location(s) of lesion
1. UMN signs in TL and PL	Cervical cord or brain
2. LMN signs TL UMN signs PL	Lower cervical cord
3. UMN signs TL Normal PL	Cervical nerve roots or peripheral nerves in TL
4. Normal TL UMN signs PL	Thoracic or upper lumbar cord
5. Normal TL LMN signs in PL	Lower lumbar/sacral cord, or cauda equina, or peripheral nerves in PL
6. LMN signs TL and PL	Peripheral polyneuropathy

TL = thoracic limb UMN = upper motor neuron-type deficits
PL = pelvic limb LMN = lower motor neuron-type deficits

LMN signs in a limb can be caused by lesions within the vertebral canal damaging the cell bodies, proximal motor axons and ventral nerve roots, or by more peripheral, extraspinal problems. Bilateral signs do not always indicate a central lesion, as many polyneuropathies are bilaterally symmetrical. Extraspinal problems are less likely to be associated with urinary or faecal signs.

Localisation of Sensory Signs

In some spinal and peripheral disorders, ataxia is the predominant sign. This results from defects in proprioceptive transmission to or within the CNS or within the central co-ordinating unit - the cerebellum. In this chapter we will be concerned with localisation of spinal and peripheral forms.

Where a peripheral nerve problem is causing ataxia, it is likely that there will also be conscious proprioceptive deficits, loss of muscle tone and depression or absence of the patellar reflex (Figure 3.2 and Table 3.2). The pedal reflex and pain sensation are usually spared, as they are mediated by small diameter fibres on the afferent side. Using the presence or absence of tone and tendon reflexes it should be possible to distinguish spinal and peripherally located ataxia. With an ataxia of spinal origin, there may be additional signs such as those involving the panniculus reflex, sympathetic function etc., as listed in Table 3.4. Whether such localising signs are present or not depends largely on the pathological changes. Gross tissue destruction due to injury, compression or inflammation will often show localisation while more subtle degenerative disorders do not.

Estimating the Severity of the Lesion

There is no all-embracing strategy for estimating the severity of damage applicable to every type of condition. The severity at any particular stage is judged by the degree of functional deficit, which may not be a static parameter but can increase or decrease as the lesion progresses or resolves. In essence, the cord consists of white and grey matter and, while a gross oversimplification, the white matter can be regarded as transmitting impulses cranially or caudally, and the grey matter as relaying these impulses to and from the periphery.

Using this scheme the clinically-important segments of grey matter are those innervating the limbs, respiratory muscles, bladder and sphincters - essentially the cervical and lumbar enlargements. Damage to these segments will denervate clinically-important muscles. The severity can be judged by the degree of LMN damage - paresis or paralysis, depressed or absent reflexes and the amount of atrophy. As neurons are not replaced, any marked or progressive loss will have serious consequences.

In evaluating white matter damage, we need to choose assessable functions that are normally transmitted across the damaged segment. Usually, motor and bladder function, and deep pain sensation are used. With increasing severity of damage these functions tend to be impaired and lost in that order. This scheme

Table 3.4: Signs used for localisation of lesions

The signs listed are those useful for localisation and not the entire range of signs, e.g. loss of bladder control could occur depending on the severity of the lesion but would not be particularly useful localising signs. It is also possible that some or all of the signs might not be present in certain conditions.	
	Cranial cervical cord
Motor	UMN in TL and PL (sometimes TL more severe than PL).
Sympathetic	Horner's syndrome. Skin hyperthermia over head and body.
Others	Neck pain/stiffness
	Caudal cervical cord
Motor	UMN in PL LMN in some muscles of TL
Sympathetic	Horner's syndrome. Skin hyperthermia over head and body.
Panniculus reflex	Absent if C_8/T_1 involved
Sensation	Loss of pain sensation is unlikely in cervical lesions as damage of such severity is likely to cause respiratory failure.
	Upper thoracic cord
Motor	UMN in PL TL possibly normal, or Schiff-Sherrington phenomenon could be present in severe lesions.
Sympathetic	Skin hyperthermia behind lesion
Respiration	Paradoxical
Panniculus	Restricted to area immediately caudal to shoulder
Sensation	May also be restricted
	Middle and lower thoracic cord, and L_1
Motor	UMN in PL TL normal
Sympathetic	Skin hyperthermia behind lesion
Panniculus	Cut-off at level of last intact dermatome
Sensation	May also be restricted
	L_2 and L_3
Motor	UMN in PL TL normal
Panniculus	Intact
Sensation	May also be restricted
	L_4 - sacral segments
Motor	LMN in some muscle groups of PL
Anal reflex	Lost if sacral segments involved
Sensation	May be restricted in dermatomal distribution over limbs
	Cauda equina syndrome*
	Mild distal PL weakness and proprioceptive deficits Urinary and faecal incontinence Loss of anal reflex Paralysis and anaesthesia of tail Loss of perineal sensation Lumbosacral pain *The combination of signs will vary with the cause of the problem.

Table 3.5: A system for evaluating the severity of white matter damage to spinal cord segments following injury or compression. It is based on assessment of bladder function and deep pain sensation behind the level of the lesion.

1	Weakness. varying from mild to severe paresis.
2	Paralysis. Paraplegia or tetraplegia of an UMN type.
3	Paralysis (as in 2) and loss of bladder control (usually urinary retention and overflow).
4	Paralysis and loss of bladder control (as in 3) and loss of deep pain sensation. (This lever of severity is not usually compatible with survival in cervical cord injuries).

is particularly useful for cord injuries and compression, and such cases can be graded as in Table 3.5.

Cervical cord injury or compression often causes less severe signs than lesions in the thoracolumbar area. One obvious reason is the different vertebral canal/spinal cord diameter ratios. It is highly likely that a cervical cord lesion with loss of pain sensation caudally would also be associated with respiratory failure. Cervical cord damage often results in motor deficit (tetraparesis or tetraplegia) and occasionally in loss of bladder control. Damage to the cervical enlargement will also cause grey matter destruction and LMN signs in the thoracic limbs. As mentioned above, this often has more serious consequences than damage confined solely to white matter.

In thoracolumbar lesions (e.g. disc herniations) we are concerned essentially with white matter damage, the severity of which is judged as described above in Table 3.5.

In injuries and compressions, the prognosis usually correlates with the severity and the scheme indicated in Table 3.5 will provide a good guide of this damage. However, this system cannot be transferred directly to other disease categories such as inflammatory and degenerative myelopathies. For example, a dog with a disc herniation could be paraplegic and recover completely, whereas dogs with viral myelitis or CDRM might only be paretic and yet have a very poor or hopeless prognosis.

Reference

Wheeler SJ & Sharp NJH (1994) Patient examination. In *Small Animal Spinal Disorders: Diagnosis and Surgery*. Mosby-Wolfe, London, 21-30.

CHAPTER FOUR

Ancillary Diagnostic Aids

INTRODUCTION

This chapter covers some of the ancillary diagnostic aids available to the clinician, which are useful in the identification of nervous system diseases.

Following the determination of the nature of the lesion (i.e. whether or not it is neurological) and location of the lesion (from the neurological examination), the next stage is to identify the disease process. This is the role of the ancillary diagnostic aids.

Some of these aids, typically radiography and clinical pathology are available widely. Others, particularly the electrophysiological techniques are only found in larger centres.

Part 1 Haematology, Biochemistry, Cerebrospinal fluid analysis, and other clinicopathological investigations.

The widely available techniques that form part of the minimum database in most patients.

Part 2 Electromyography and nerve conduction studies.

Electrophysiological techniques required for full evaluation of diseases of peripheral nerve and muscle.

Part 3 Urodynamic studies.

Electrophysiological techniques for evaluation of the lower urinary tract.

Part 4 Muscle and nerve biopsy.

Invasive techniques for the collection and evaluation of tissue samples.

CHAPTER FOUR - Part One

Haematology, Biochemistry, Cerebrospinal Fluid Analysis and other Clinicopathological Investigations

Richard J. Evans

THE ROLE OF CLINICAL PATHOLOGY IN NEUROLOGICAL INVESTIGATION

Clinical pathological determinations have two roles in the investigation of patients presenting with signs of nervous dysfunction. In some cases, apparent nervous signs will be due to disturbance of neural or muscular function secondary either to systemic disease or to a generalised metabolic disturbance. In such cases, clinical pathology is essential in the identification of the underlying cause and this is the major role for such tests.

Clinical pathology is limited in value in diseases which directly involve nervous tissue. Cerebrospinal fluid (CSF) examination is the most valuable investigation when CNS signs are present, although even this has limited value. Much of this chapter is concerned with the collection and examination of CSF and interpretation of the findings.

Diagnostically helpful changes in the peripheral blood are seen rarely in primary neurological conditions. Faecal examination is rarely helpful, as parasitic infections that affect the CNS are generally not patent at the time when neurological signs become apparent.

The occurrence of seizures or tetany, episodic or persistent weakness, collapse, coma, or of multifocal or variable neurological signs are all circumstances in which the clinician should investigate the possibility of an underlying generalised or systemic disease being present (see Table 4.1). Clinical pathological investigation may also be required to monitor the consequences of nervous or muscular diseases.

Clinical Pathology in Generalised Disorders Inducing Neurological Signs

The generalised disorders that may induce or mimic nervous dysfunction may be divided into seven overlapping categories:

1) Inflammatory disease.
2) Haematopoietic neoplasia involving the CNS.
3) Disturbance of oxygen transport - see Table 4.1.
4) Disturbance of intermediary metabolism - see Table 4.1.
5) Disturbance of body fluid homeostasis - see Table 4.1.
6) Intoxications.
7) Diseases of muscle.

GENERAL CLINICAL PATHOLOGY

Haematological examination

Haematological examination is of value in all patients where inflammatory disease or haematopoietic neoplasia are suspected as the cause of neurological signs. These disorders can result in well-documented haematological changes (see haematology textbooks for discussion). In focal inflammatory disorders, changes may or may not be present in the peripheral blood. Haematological examination may reveal a leukocytosis in encephalitis, abscess and particularly in meningitis. Fungal and protozoal infections may be associated with leukocytosis or with normal white cell values in peripheral blood. Leukopenia progressing to leukocytosis may be encountered in toxoplasmosis. In feline infectious peritonitis (FIP), generally there is a mild neutrophilia with a left shift, a moderate non-regenerative anaemia, and hypergammaglobulinaemia. Leukopenia may be due to underlying bone-marrow disorders, and may be associated with distemper or overwhelming bacterial infections.

Care must be exercised in interpretation of haematological data. Absence of haematological changes does not rule out inflammatory nervous system disease. Occasionally haematopoietic neoplasms may involve the meninges or CNS parenchyma, but will not invariably be detectable by routine haematological examination. When present, haematological changes may result from treatment rather than disease. Most common is the stress leukogram induced by glucocorticoid therapy. More unusual changes may also be encountered, for example, haemolysis and disseminated intravascular coagulation can result from muscle damage occurring during surgery.

Table 4.1: Systemic derangements presenting with neurological signs

Disturbance	Neurological signs	Associated signs	Underlying conditions
1. OF OXYGEN TRANSPORT			
Hypoxia	Neuromuscular weakness Ataxia Collapse Seizures Coma	Cyanosis (generalised hypoxia only)	Cardiac insufficiency Haemorrhage Vagal syncope Airway obstruction Severe anaemia Toxic conversion of haemoglobin to derivatives not supporting oxygen transport (e.g nitrate or paracetamol poisoning) Hyperviscosity Vascular spasm Thrombosis Embolism
Blood hyperviscosity	Episodic variable neurological signs Transient disorientation Transient weakness Transient collapse Convulsions	Polydipsia	Polycythaemia Plasma cell myeloma (IgM secreting) Haemagglutinin disease
2. OF INTERMEDIARY METABOLISM			
Hyperglycaemia / hyperosmolarity / keto-acidosis	Depression Neuromuscular weakness Coma	Polydipsia / polyuria Shock	Uncontrolled diabetes mellitus
Hypoglycaemia	Dullness / depression Neuromuscular weakness Collapse Seizures Coma		Insulinoma Insulin overdose Hypoadrenocorticism Hepatic failure Glycogenosis Starvation Neonatal glycogen depletion Strenuous exercise
Hyperammonaemia	Depression Aimless walking Head pressing Hysteria Aimless / unpredictable aggression Cortical blindness (may be transient) Seizures Coma *Signs may be prominent after high-protein meal*	Anorexia Polydipsia / polyuria Vomiting Diarrhoea Bleeding tendency	Hepatic failure (acute or chronic) Congenital portosystemic shunts Acquired portosystemic shunts
CNS hereditary metabolic disorder	Varied	Varied	Specific genetic deficiencies

Table 4.1: continued

3. OF BODY FLUID HOMEOSTASIS

Hyperosmolarity	Depression Neuromuscular weakness Seizures Coma		Severe dehydration Hypernatraemia Hyperglycaemia Uraemia
Hypernatraemia	Neuromuscular weakness Paresis Seizures Coma	Oliguria / anuria Polydipsia (once access to water permitted) Polyuria /(± polydipsia)	Severe dehydration Excess dietary sodium intake coupléd with water restriction Diabetes insipidus or mellitus plus water restriction
Hyponatraemia	Disorientation Neuromuscular weakness Incoordination Collapse Seizures	Anorexia Shock ± Cyanosis **With diminished extracellular fluid volume** Low pulse volume Decreased skin turgor Sunken eyes **With expanded extracellular fluid volume** Generalised or pulmonary oedema	Vomiting Diarrhoea Over-vigorous diuresis Hypoadrenocorticism
Hyperkalaemia	Depression Disorientation Neuromuscular weakness Paralysis	Anorexia Vomiting Diarrhoea Ileus Bradycardia Weak pulse Cardiac arrest	Hypoadrenocorticism Renal failure Urinary tract obstruction Acidosis Iatrogenic (potassium-containing infusions) Muscle necrosis
Hypokalaemia	Dullness / depression Disorientation Severe neuromuscular weakness Tetany	Polyuria / polydipsia Cardiac arrhythmias Failure of urine concentration	Vomiting Diarrhoea Insulin administration Potassium-losing diuretics High-dose corticosteroid therapy Hyperaldosteronism Acute renal failure
Hypercalcaemia	Depression Neuromuscular weakness	Polyuria / polydipsia Nephrocalcinosis Renal failure Lameness / bone pain / pathological fractures Cardiac arrhythmias	Vitamin D toxicosis Primary hyperparathyroidism Lymphosarcoma Multiple myeloma Other osteolytic neoplasms Dietary calcium excess
Hypocalcaemia	Tetany Weakness Seizures	Dependent on aetiology	Lactation tetany Hypoparathyroidism Iatrogenic (2° to thyroid surgery) Acute pancreatitis Ethylene glycol poisoning Oxalate (e.g. rhubarb) poisoning
Uraemia	Depression Muscle weakness Tremors Seizures Tetany	Anorexia Vomiting Diarrhoea Uraemic odour Failure of urine concentration Polyuria / polydipsia Oliguria /anuria Anuria	Compensated chronic renal failure Decompensated chronic renal failure Pre-renal failure Early acute renal failure Post-renal failure/ bladder rupture

When distemper encephalitis is suspected, examination of a buffy coat preparation (or a conjunctival smear) for inclusion bodies may be of value, although these have often disappeared by the time the animal shows neurological signs.

Routine haematological examination may reveal the presence of polycythaemia or of the greatly increased plasma protein concentration seen in plasma cell myeloma. Each of these abnormalities may give rise to neurological signs secondary to hyperviscosity of the blood and altered CNS perfusion.

Serology

In some cases of inflammatory disease, serology may be of assistance. When toxoplasmosis or neosporosis are suspected, determination of antibody titres to the respective organisms may be valuable. Titres of antibody against FIP virus may also be of some value in cats in which this disease is suspected, but their interpretation remains controversial and requires considerable care. Examination for feline leukaemia virus (FeLV) antigen and for feline immunodeficiency virus (FIV) antigen or antibodies should be performed for all cats presented with obscure neurological signs, in view of the high frequency of these infections and their possible neurological presentations.

Biochemical investigations

A variety of systemic disorders may result in functional neurological signs (Table 4.1) and are often detectable by biochemical examination of the blood.

Hepatic function

Hepatic failure with hyperammonaemia may result in encephalopathy. Where this is suspected, liver state and function should be investigated. Because it is liver functional capacity which is critical, liver enzymes, which reflect the state of the liver rather than its function, are of limited value. True indices of the liver's functional capacity are much more helpful. Plasma bile acid determinations are now readily obtainable and are of particular value, as elevations in concentration are a very sensitive indicator of reduced hepatic functional capacity (Evans and Heath 1988).

In most circumstances fasting bile acid values are employed, but in portosystemic shunting, post-prandial values are more reliably elevated. Also, the albumin concentration may be lowered, cholesterol concentration and the one stage prothrombin time may be increased; together these findings provide useful evidence of liver dysfunction.

Assessment of sulphobromophthalein (BSP) clearance has now essentially been supplanted by bile acid determinations. Blood ammonia estimation has been used to detect hyperammonaemia, but there are considerable difficulties in achieving this reliably (Evans and Heath 1988). In such cases, ammonium biurate crystals may be present in the urine. Liver biopsy is required to establish the nature of the hepatic disease.

Uraemia

Seizures may occur in severe uraemia. Determination of plasma urea, creatinine and phosphate will confirm this suspicion.

Glucose

Both hyperglycaemia and hypoglycaemia may give rise to coma, thus the determination of blood glucose is essential in the comatose animal. Urine analysis will reveal the presence of glycosuria in hyperglycaemic coma, and of ketonuria in ketotic coma. In severe hyperglycaemia, hyperosmolarity may contribute to the coma and measurement of plasma osmolality may be helpful.

Transient hypoglycaemia in cases of insulinoma or other causes of hyperinsulinism and in glycogen storage diseases may give rise to collapse. In cases of insulinoma, the fasting blood glucose is low and the amended insulin:glucose ratio (AIGR) raised. Assay of plasma glucose at the time when signs are manifest is important in animals with episodic weakness or collapse.

Electrolytes

Hyponatraemia may give rise to muscle weakness. It may result from hypoadrenocorticism and from overzealous diuretic therapy.

Hyperkalaemia may give rise to listlessness, disorientation, neuromuscular weakness and severe abnormalities of cardiac conduction, which can be fatal. In primary hypoadrenocorticism (Addison's disease) and iatrogenic Addisonian crises, following abrupt withdrawal of glucocorticoid therapy, profound hyperkalaemia is encountered. It may be also associated with acidosis, renal failure, diabetes mellitus and severe dehydration.

Hypokalaemia is becoming increasingly recognised as an important cause of depression and muscle weakness, particularly in the anorexic cat. It also occurs as a result of gastroenteritis, in renal dysfunction, during therapy with potassium-losing diuretics and in Conn's syndrome (hyperaldosteronism).

Hypokalaemia with associated polymyopathy occurs as a rare episodic familial condition in Burmese cats. In patients where plasma potassium concentration is abnormal, detailed consideration must be given to overall ionic and acid base-balance. Plasma concentration of potassium may be misleading as to total body reserves, because of shifts of the ion between plasma and intracellular fluid. Hypocalcaemia may give rise to tetany, which may be confused with seizures or tetany of neurological origin.

Other

Blood lead determinations are of value in suspected lead poisoning.

Urine analysis

The situations in which analysis of urine is of value are limited. The finding of urine of specific gravity below 1.007 raises the suspicion of diabetes insipidus, possibly central in origin. This possibility may be investigated further by performing a water deprivation test. The finding of glucose in urine suggests that significant hyperglycaemia is present (but care in Fanconi syndrome), and ketones indicate the presence of ketoacidosis. Ammonium biurate crystals may be present in the urine of animals with hepatic dysfunction.

CEREBROSPINAL FLUID EXAMINATION

Changes in the composition of the CSF may reflect the involvement of the CNS parenchyma, the meninges, the choroid plexus, the nerve roots, or the axial skeleton in a disease process. However, the conditions where CSF examination will provide useful diagnostic information are limited. In a significant proportion of cases of inflammatory disease and of neoplasia it may be useful. In trauma, haemorrhage, degenerative disorders, spinal cord compression and hydrocephalus, CSF examination may provide helpful information but other investigations are required. In many cases, it still will not be possible to establish the diagnosis unequivocally by CSF analysis. Patients need to be selected with care if maximum benefit is to be gained from its use. It is important to consider the history, the clinical signs and the results of physical and neurological examinations to identify the type of disease likely to be present before performing a CSF collection.

Indications and Contradictions

The main indications for analysis of CSF are suspicion of inflammatory disease or neoplasia, although failure to find tumour cells does not rule out the possibility of neoplastic involvement. It should be remembered that collection of CSF is not without risk.

There are several contraindications to the collection of CSF, which fall into three main categories:

Anaesthetic risk

This is the most common contraindication. Any situation where general anaesthesia is considered unnecessarily risky is a contraindication to CSF collection.

Circumstances that may lead to mechanical trauma to CNS tissue or nerve roots

Raised intracranial pressure predisposing to brain herniation may be evident on examination by evidence of papilloedema or by progressive disorientation leading to profound depression, pupillary dilation and coma. The performance of a CSF tap in the face of raised intracranial pressure may lead to brain herniation, either of the caudal cerebral cortex under the tentorium cerebelli, or of the brain stem and cerebellum through the foramen magnum.

Factors predisposing to mechanical trauma to CNS tissue during CSF collection include:

Instability of the bony structures surrounding the puncture site. Fractures of the cranial cervical region or skull, or subluxations or congenital malformations of the cervical vertebrae render the neuraxis and adjacent nerve roots liable to trauma during the manipulations necessary for CSF collection from the cerebellomedullary cistern ("cisterna magna"). Fractures, subluxations or congenital deformities in the lumbosacral region may similarly result in the spinal cord, cauda equina or spinal nerve roots being injured during CSF collection.

Lesions which distort or alter the anatomical disposition of the brain stem or the caudal spinal cord. Foramen magnum herniation or local space-occupying lesions may so alter local anatomy, thus predisposing the brain stem to trauma by the spinal needle. Such lesions should be suspected where there is paralysis of cranial nerves nine to twelve, where there are progressive changes of pupillary diameter or the degree of consciousness, or where there is anisocoria of central origin. In lumbar CSF collection, it is commonly held that transfixion of the lumbar spinal cord by a spinal needle is of no clinical significance. However, local anatomical distortions may again increase the severity of such trauma.

Known or suspected intracranial haemorrhage

In the presence of haemorrhage, further bleeding may be induced by manipulation or CSF withdrawal, which may itself lead to herniation or to meningeal irritation, worsening the signs and prognosis.

Equipment

For the collection of CSF, a spinal needle with a stilette usually is used. A 20 gauge, 1.5 inch needle, is used for most patients. Smaller needles may be needed in very small dogs and cats, and larger needles may be used in giant breeds. A syringe and sample collection pots (see below) also should be to hand.

If CSF pressure is to be measured, a three-way tap and CSF manometer are required. However, the value of this determination is very doubtful.

Collection Technique

In small animals, the cerebellomedullary cistern is often the site of choice for collection of CSF samples, although lumbar collection sites may also be used. General anaesthesia is required for the great majority of CSF collections and strict asepsis is essential.

Collection from the cerebellomedullary cistern

Anaesthesia is induced and the patient intubated, preferably with a kink-proof endotracheal tube. The caudal aspect of the vault of the skull and the dorsal aspect of the neck should be clipped to a level well behind the dorsal spine of the axis. The patient is positioned in lateral recumbency with the occiput and dorsum of the neck parallel and close to the edge of the table. For a right-handed operator, the animal should be placed in right lateral recumbency. The skin is prepared and the operator should scrub hands and don sterile gloves. An assistant holds the head so that the neck is flexed at a right angle with the sagittal axis of the skull parallel to the table surface (Figure 4.1). Adoption of this position may kink the endotracheal tube, so it may be wise to deflate the cuff at this stage.

Figure 4.1: Position for CSF collection from the cerebellomedullary cistern ("cisterna magna")

There are two methods available for identifying the site for puncture, both requiring the correct identification of certain landmarks (Figure 4.2). The bony prominence of the occipital protuberance is palpated. The longitudinal midline runs from this point to the dorsal spine of the axis and is identified as a groove in the soft tissues of the dorsal aspect of the neck. The wings of the atlas also are identified. Here the methods of cisternal puncture vary importantly and are described separately.

Method 1

An imaginary line is drawn between the wings of the atlas, and the point where it transects the midline is noted. The site for puncture is in the midline, midway between this point and the occipital protuberance, and slightly caudal to a depression in the soft tissues which lies just behind the protuberance. (It is a temptation to make the puncture in this depression, but doing so invariably leads to the needle hitting bone.) The needle is inserted perpendicular to the skin and advanced.

Method 2

The point of insertion of the needle is the intersection of the line joining the wings of the atlas and the dorsal longitudinal midline. The needle is inserted at an angle such that the point is directed rostrally, toward the angle of the jaw, and advanced in this direction.

The two methods are designed to achieve the same result, although there are significant differences in the methods and one should be selected and adhered to. The needle is advanced through the layers of soft tissue until the dura mater is penetrated and the subarachnoid

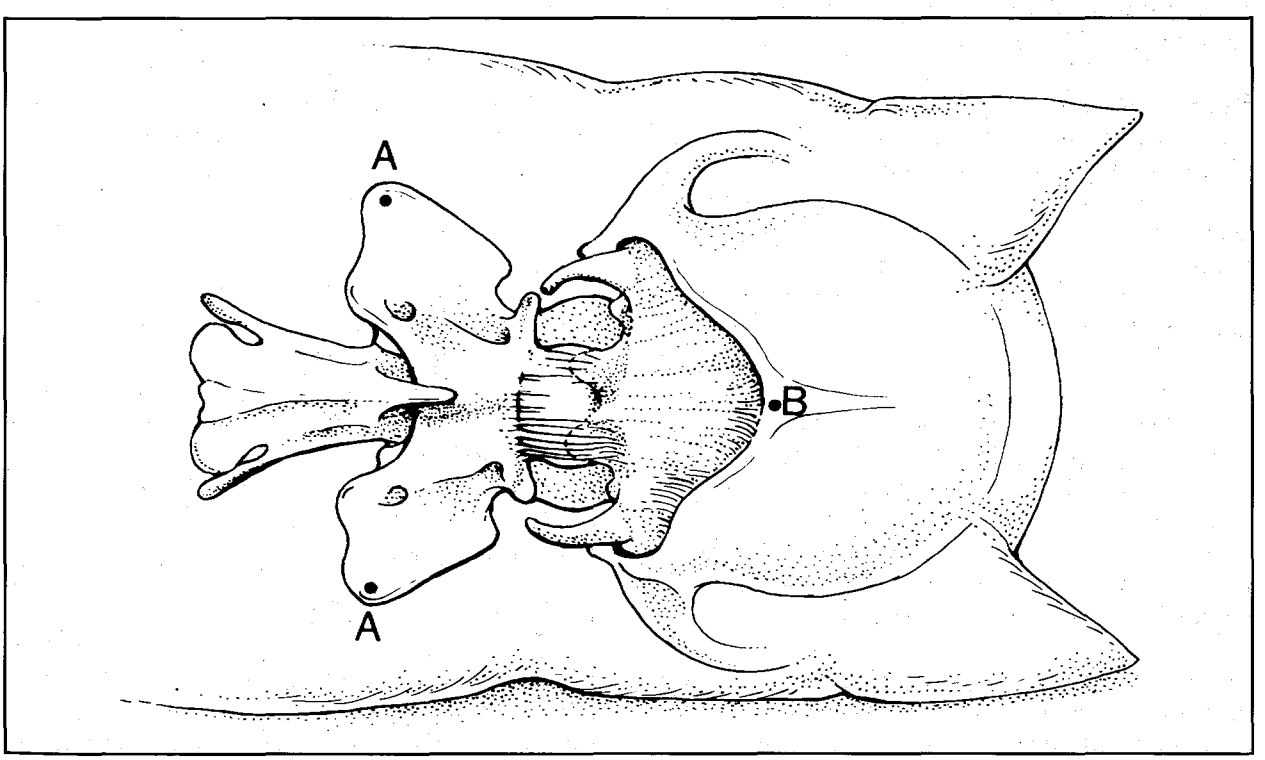

Figure 4.2: A - prominent wings of atlas B - Occipital protuberance

space entered. It is important to know where the point of the needle is relative to the dura mater, and this can be achieved in one of several ways. A popping sensation is felt when the needle penetrates the atlanto-occipital membrane and the dura mater in many patients, although this is not universal. Thus, using this as the only estimate of depth may lead to the needle being advanced too far, penetrating neural tissue with potentially catastrophic results. It is suggested that each time the needle is advanced the stilette is removed to ascertain whether CSF flows. Alternatively, once the skin and superficial soft tissues are penetrated, the stilette may be removed and the needle advanced, the hub of the needle continually being observed for the appearance of CSF. Whilst this method carries the theoretical risk of a soft tissue plug obstructing the needle and preventing CSF flow, this is considered the safest by many. Should the needle hit bone, either it may be "walked" off the bone or it may be withdrawn completely and a fresh attempt made. If dark, venous blood appears in the needle, the needle is usually lateral to the midline and should be repositioned.

Collection from the lumbar spine

Cerebrospinal fluid collection may be performed by puncture of the subarachnoid space in the lumbar region (Kornegay 1981). The procedure may be performed with the animal either in lateral or in ventral recumbency, although the former is usual. The skin is clipped and prepared and the animal is positioned with the spine flexed. In the dog, the needle is introduced in the L_5-L_6 intervertebral space, and in the cat at the L_6-L_7 space, in each case just cranial to the appropriate spinous process. The needle is advanced perpendicularly, redirecting it should it hit bone, until CSF flows. In this way, a sample is collected from the dorsal subarachnoid space. Alternatively, the needle may be passed through the nervous structures to the floor of the vertebral canal, and CSF collected from the ventral subarachnoid space. The former method is preferable. The technique is more difficult than cerebellomedullary cistern puncture.

Selection of site

As mentioned, collection of CSF is more difficult from the lumbar spine, and blood contamination (which makes interpretation difficult) is much more likely. These disadvantages must be weighed against the higher diagnostic yield of lumbar fluid samples in spinal cord lesions (Thomson, Kornegay and Stevens 1990).

Collection of samples

Whichever site is used, once CSF flows freely, samples may be collected. It is preferable to allow the CSF to drip from the needle into collection pots. Occasionally, it may be necessary to apply gentle syringe suction to collect a sample, particularly in small patients and in the lumbar spine. In such cases, the collection should be by very slow withdrawal, as the application of significant suction increases the likelihood of haemorrhage. If there is initial blood contamination, particularly with passive flow, allowing the flow to continue and discarding the early portion of fluid usually will allow the collection of an uncontaminated specimen. Should this fail, the needle should be removed and the tap repeated, possibly on a different occasion. Blood contamination makes meaningful laboratory examination extremely difficult. Failure of CSF flow generally is due to incorrect needle placement, although lowered pressure resulting from anaesthesia may be responsible. In some cases, although flow begins, it ceases before an adequate sample is collected.

Normal CSF is low in protein and cell content, does not clot and can be collected in sterile plain tubes. In disease, the cell count may be higher and bacteria may be present, protein concentrations may be high and the presence of fibrinogen may lead to clotting. Therefore, it is wise to be prepared to collect CSF into EDTA pots for cytology and into oxalate/fluoride pots if glucose concentration is to be determined. Sterile plain pots are required for microbiological investigation. Paediatric 1 ml pots should be used because of the small volumes of fluid available. If the specimen is to be sent to a laboratory for cytological examination, it must be preserved by the addition of an equal volume of 4% formalin solution, or of 50% or 95% ethanol. Alternatively, smears may be made by one of the techniques described below. They either may be air-dried, or fixed for 10-20 minutes in absolute ethanol, and the laboratory informed of which method is used.

Laboratory Examination of CSF

This consists of evaluation of the following:

- Colour
- Turbidity
- Specific gravity
- Protein concentration
- Presence of globulins (Pandy, Nonne-Apelt or quantitative examination)
- Red cell count
- Nucleated cell count and differential count
- Coagulation

The colour and turbidity of the fresh specimen are most easily assessed and recorded by the clinician at the time of collection. Where infection is suspected the following additional investigations may be performed:

- Culture
- Gram stain
- Ziehl-Neelsen stain
- Indian ink or other negative staining
- Glucose concentration determination.

Measurement of CSF glucose is most valuable when accompanied by determination of plasma glucose.

Techniques of Examination

Colour

This is assessed by inspection against a uniformly illuminated, plain white background and compared with distilled water.

Turbidity

This is assessed by visual examination. If discolouration makes the judgement difficult, placing a pencil or ruler behind the specimen is helpful. In clear but discoloured samples, the outline of the object and the printing on it will be clearly perceptible. If there is turbidity, these features will be obscured.

Cell counts

Cell counts are performed using an improved Neubauer haemocytometer, unless the cell counts are extremely high, in which case a Coulter or other automatic cell counter may be used. When using the haemocytometer method, the fluid may be counted without dilution, or after dilution by 1 in 10 or greater with white cell counting fluid, depending on the cellularity. Both sides of the chamber are filled. It is important not to introduce air bubbles or to allow fluid to spill over into the troughs. Red cells and nucleated cells usually are distinguishable by their appearance. In cases of doubt, a little crystal violet or methylene blue may be added to the counting fluid. It then will be possible to identify white cells by their stained nuclei. The cells in all nine of the large squares making up the ruled area of the chamber are counted on each side and the mean calculated. If the count was made using undiluted CSF, the result is multiplied by 1.1 to calculate the cells per microlitre (µl). If there was dilution, the result must be multiplied by (1.1 x dilution factor) to obtain the count.

Cytological examination

The nucleated cells may be differentiated by examination of stained smears. The stains commonly used are the Romanowsky stains used for blood films (Giemsa, May-Grunwald-Giemsa, Leishman's, Wright's). Cells are very labile in low protein fluids such as CSF, and specimens for cytological examination must be prepared within 30 minutes of collection, or the material must be fixed. Smears may be prepared by one of a number of techniques:

Centrifugation of the specimen in a conical centrifuge tube (80-100g for 5 minutes) followed by resuspension of the sediment in 100 µl of autologous serum. The resuspended sediment is smeared using a spreader to pull the fluid along the slide, as in the preparation of a blood film.

Sedimentation of the cells directly on to the slide from the CSF sample may be achieved in two ways:

> ***Passive gravitational sedimentation*** - A flanged cylinder about 1-2 cm in diameter and 1-2 cm high is applied to a slide and anchored to it with a ring of silicone grease. (A suitable cylinder may be prepared from the barrel of a 5 ml syringe). An intervening filter paper in which a hole has been made to match the internal diameter of the cylinder may be used to absorb the fluid with the cylinder attached to the slide with bulldog clips. CSF (1-3 ml, depending on cellularity and the capacity of the cylinder) is put into the cylinder and the assembly placed in a refrigerator for two hours. During this time, any cells will sediment out and adhere to the slide. The cylinder and filter paper (if used) are removed and the slide dried, fixed and stained in the usual manner.
>
> ***Cytological centrifuge*** - This method only will be available in large laboratories with a considerable throughput of samples.

Direct smearing, as for blood films, is applicable only to samples of extremely high cellularity.

Approaches not involving the use of fixed, stained smears

Wet preparations under a coverslip may be examined by dark field or phase contrast microscopy, or by transmitted light after the addition of methylene blue. This is an insensitive technique and is suitable only for highly cellular samples. The cells are clustered rather than spread out, making differentiation difficult.

Membrane filtration may be employed to deposit the cells on Millipore or similar filters. The cells from a large volume of CSF are concentrated and trapped in the filter, but again they are clustered together. Romanowsky stains cannot be used and these preparations commonly are stained by Papanicolaou's method, or with haematoxylin and eosin. Differentiation of the cells requires more experience than with Romanowsky-stained smears and can be particularly difficult for tumour cells. This technique is suited best to referral laboratories, particularly for samples sent as fixed suspensions in formalin or methanol.

Having prepared the smear, a differential count should be performed. In smears from normal animals, and in many cases of CNS or meningeal disease, few cells will be present, even after concentration. In such cases, all available cells on the smear must be examined and included in the differential count. A few pathological samples will have sufficient cells present for a differential count to be made on one or two

hundred cells. Differentiation is made using the same morphological criteria and nomenclature as for cells in the blood. Macrophages or tumour cells may be encountered in some specimens.

Specific gravity
In view of the limited sample volumes available, specific gravity is best determined using a refractometer. The sample should be centrifuged to remove any suspended cells and the supernatant used.

Protein concentration
The concentration of protein in the CSF is low compared with plasma and an approximate determination may be made using dipsticks of the type used for assessing urine protein. Increased total CSF protein may be detected qualitatively by shaking the sample. In normal circumstances, a very slight amount of foam, if any, is formed and any that does develop breaks down within five minutes. Increased protein levels result in moderate to marked foam formation and the foam is stable for over five minutes.

Accurate determinations of CSF protein concentration may be made by the Coomassie blue dye-binding method or by turbidimetry with sulphonylsalicylic acid (SSA) or trichloroacetic acid (TCA). These methods require careful calibration and quality control and are limited to referral laboratories.

Globulins
Normally, the majority of CSF protein is albumin, and in pathological states increases generally are due to globulins. The detection of globulins is often performed using a qualitative test.

The Pandy test. A solution of 10 mg of carbolic acid crystals is made in 100 ml of distilled water, and one drop of this phenol solution is placed in a small test tube. A single drop of CSF is added and the mixture examined visually. With normal CSF, the mixture remains clear, although a faint inhomogeneity may be detectable, this being a negative result, which is given a score of 0. Where globulins are increased, definite white or grey turbidity develops, which is qualitatively scored on a scale of 1+ to 4+.

The Nonne-Apelt or Ross-Jones test. 1ml of saturated ammonium sulphate solution is put into a small test tube and 1 ml of CSF is layered carefully over this. The tube is allowed to stand for three minutes, after which it is examined visually. With normal CSF, there is no ring detectable at the interface, while in the presence of increased globulins, a grey ring of precipitate is formed.

Urine dipsticks. Dipsticks intended for the detection of protein in urine can also be used for qualitative assessment of CSF protein. False negatives and incorrect readings can occur. Caution is therefore needed in interpretation. However, a dipstick reading of 100 mg/dl or more can certainly be regarded as indicating a need for further investigation.

Any of the qualitative determinations should be followed-up by quantitative measurement of globulin concentration, if an abnormality is suspected on the basis of the screening test.

Quantitative determination of globulins. This is made by electrophoresis after concentration of the sample by dialysis against glycerol. The results are unreliable quantitatively but qualitative examination of the trace from scanning the electrophoresis strip will give some indication of the extent of globulin increase and of the fractions present.

Coagulation
This occurs in the presence of fibrinogen and is detected visually. Fibrin strands or a solid coagulum may be seen.

Glucose
Glucose concentration may be measured by any technique applicable to blood, glucose oxidase methods being the most specific.

Approximate values can be obtained using dipsticks intended for the measurement of plasma glucose. CSF glucose determinations are of most value if combined with simultaneous determination of plasma glucose.

Microbiology
In bacterial, fungal or protozoal meningitis, encephalitis or myelitis, organisms may be present in the CSF. Microscopic examination of sedimented smears stained by the Gram and the Ziehl-Neelsen methods may be of value. In the case of yeast infections, Indian ink or nigrosin may reveal organisms by negative staining. Micro-organisms also may be encountered when making cytological examination of Romanowsky stained smears.

Bacterial or fungal culture is indicated when the CSF is turbid, clots are present, the nucleated count is high or when organisms are seen on stained smears. Culture is most likely to be successful using large quantities of CSF placed in blood culture bottles.

CSF enzymology
There are reports of the determination of CSF enzyme concentrations (see Coles 1980 for review).

Any leakage of these enzymes from damaged brain tissue is confined to CSF and there is no effect on levels measured in plasma or serum. However, the changes encountered are small and correlate poorly with the pathological process and are of limited value.

Normal Findings for Cerebrospinal Fluid

If normal, the CSF is colourless and free from turbidity, resembling water. The nucleated cell count of cerebellomedullary CSF in the normal dog is less than 5 per microlitre. The cells encountered are predominantly lymphocytes, although occasional macrophages or monocytes will be seen. Normal CSF is free of micro-organisms and sterile on culture. The specific gravity of normal canine and feline CSF is in the range of 1.004 - 1.006. The total protein concentration of cerebellomedullary cistern CSF is in the range of 8-30 mg/dl in the dog and 8-20 mg/dl in the cat, but lumbar samples have a higher level of protein (Bailey and Higgins 1985). Albumin comprises 80-95% of the total protein, the residue being globulins. There is no fibrinogen in normal CSF and it does not clot. The glucose concentration is in the range of 2.7-4.2 mmol/l in dogs and 3.2-4.3 mmol/l in cats, and is approximately 80% of the plasma glucose concentration.

Abnormal CSF Findings and their Intepretation

Appearance

Discolouration - the most commonly encountered is the bright red of fresh blood and usually indicates contamination at the time of puncture. Such specimens are rarely diagnostic because of the difficulty in interpretation.

Dull red or brown discolouration is a rare finding and indicates recent or chronic haemorrhage preceding collection. The finding of evidence of erythrophagocytosis (see below) and of crenated red cells on cytological examination is helpful evidence. The specimen may be turbid or clear. After centrifugation, the supernatant will be clear but discoloured.

Yellow discolouration (xanthochromia) is an uncommon finding. The colouration is caused by bilirubin and indicates haemorrhage more than 48 hours previously. Possible causes are given below (see Cytological abnormalities). Xanthochromia can also be a consequence of severe jaundice, or can be associated with hydrocephalus and with very high CSF protein concentrations.

Grey or grey-green discolouration is associated with suppuration, particularly in acute pyogenic meningitis. The presence of suppuration will be confirmed by the finding of pus cells on cytological examination.

Clots or fibrin flecks indicate blood contamination, severe, often suppurative inflammation or haemorrhage. Turbidity is common, often with reddening due to the presence of blood. When white, grey or grey-green in colour it indicates the presence of cells, organisms or fibrin. The nucleated cell count must be greater than 500 cells per microlitre to render CSF turbid. Usually, this is due to suppuration, but rarely it may be due to exfoliation of tumour cells, particularly in lymphoid neoplasia. The finding of turbidity or clots is an indication for microbiological examination.

Cytological abnormalities

When large numbers of red cells are present, it is necessary to attempt to establish whether these represent pathological haemorrhage or contamination at the time of sampling. Evidence of erythrophagocytosis in the form of macrophages laden with red cells, haemosiderin or bilirubin suggests that the red cells result from pathological haemorrhage. The finding of residual xanthochromia after centrifugation of the sample also supports this conclusion. However, in many cases it can be difficult to ascertain the significance of the presence of blood. Where there is reasonable certainty of pathological haemorrhage, this may be associated with:

- Trauma
- Intracerebral haemorrhage
- Subarachnoid haemorrhage
- Severe, acute inflammation
- Acute disc extrusion with myelomalacia
- Necrotic or erosive neoplasia

Other rare causes include:

- Leptospirosis
- Cryptococcosis
- Toxoplasmosis
- Ischaemic myelopathy
- Haemostatic disorders, particularly coagulopathies.

When there is contamination with blood, it can be very difficult to evaluate and interpret the white blood cell (WBC) and protein findings. A formula relating the ratio of white to red blood cells (RBC) in the CSF to that in a simultaneous sample of blood can be applied to correct the CSF white cell count:

$$WBC_{CSF} = WBC_{observed} - \frac{(WBC_{blood} \times RBC_{observed})}{RBC_{blood}}$$

However, doubt has been cast on the general validity of this formula and it is, at best, a crude approximation (Wilson and Stevens 1977). It is preferable to wait a few days after collecting a contaminated sample to repeat the tap in the hope of collecting diagnostic CSF.

An increase in the nucleated cells of the CSF is known as **pleocytosis**. This is usually a result of increases in WBCs. When neoplastic cells are found, often it is not possible to determine the lineage to which they belong, although on occasion large numbers of neoplastic lymphocytes are present, associated with lymphoma of the CNS.

An increase solely in mononuclear cells is a relatively uncommon finding and is suggestive of:

Viral infections	Uraemia
Toxoplasmosis	Intoxications
Distemper encephalitis	Post-vaccinal reactions
Feline infectious peritonitis	Reticulosis
Granulomatous meningoencephalitis (GME)	Cryptococcosis
Other chronic infections	Discospondylitis

Fungal infections may show an increase in CSF mononuclear cells alone, but the pleocytosis they induce is rather variable.

In globoid cell leukodystrophy, the characteristic enlarged, foamy macrophages known as globoid cells may be found (Roszel, Steinberg and McGrath 1982).

An increase in neutrophils is always indicative of pathological change and may be seen in:

- Bacterial meningitis
- Bacterial encephalitis
- Bacterial myelitis
- Abscess

} "neutrophilic pleocytosis"

- Early viral infections
- Acute distemper
- Feline infectious peritonitis
- Other CNS inflammatory conditions
- Discospondylitis
- Acquired hydrocephalus
- Necrotic tumours
- GME

Meningeal diseases have the greatest effect on neutrophil counts, which are highest in purulent meningitis. The presence of neutrophils, particularly in large or increasing numbers, is an unfavourable prognostic sign.

In GME, a mononuclear pleocytosis may be seen, but in many cases up to 30% of the cells are neutrophils (Vandevelde and Spano 1977; Bailey and Higgins 1986b). FIP can result in lymphocyte or neutrophil dominated pleocytosis.

The presence of bacteria on microscopic examination or culture in the absence of neutrophils suggests that the bacteria are due to contamination of the specimen.

Eosinophils are a relatively frequent finding, but their significance often is uncertain. They can be associated with fungal and parasitic conditions, notably cryptococcosis and toxoplasmosis. However, their presence correlates poorly with the underlying pathological process (Vandevelde and Spano 1977).

Abnormal specific gravity

A specific gravity above 1.007 raises suspicions of the presence of significant pathological change, for example, "Wobbler syndrome" with chronic cord compression often is associated with values in the range of 1.009 - 1.010. Disc extrusions may show values of 1.008 - 1.012 and parenchymal disease values of 1.007 - 1.012.

Protein abnormalities

Increased CSF protein usually is due to increased globulin levels. The protein concentration may be increased in:

- Inflammation: Meningitis, Encephalitis, Abscess, Toxoplasmosis, Distemper*
- Haemorrhage
- Neoplasia*
- Seizures*
- Fever*
- Uraemia*
- Ischaemic myelopathy*
- Disc extrusion*
- Degenerative myelopathy*
- Myelomalacia*
- GME*

In the conditions marked with an asterisk (*), the protein may be increased in the absence of pleocytosis, a situation termed "albuminocytological dissociation".

Haemorrhage contributes approximately 1 mg/dl of protein to the CSF per $10^3/\mu l$ of red blood cells. The largest increases in CSF protein (up to 5 g/l), usually accompanied by severe pleocytosis, are seen in infectious meningitis. In FIP, there may be marked elevations in globulin in the CSF.

Abnormal glucose concentrations

CSF glucose concentration usually parallels that in plasma, consistently being about 80-85% of that level. Lowered values relative to plasma glucose, usually with a decrease to less than 50%, generally are indicative of pyogenic infection. Rarely, other severe inflammatory changes or advanced neoplasia may result in such a finding.

Reduced CSF glucose with maintenance of the normal ratio to plasma glucose is seen in hypoglycaemia. Increased CSF glucose, with the normal relationship to plasma glucose, is seen in hyperglycaemia or diabetes mellitus. Slight increases are seen in some cases of encephalitis, in brain abscess, with spinal cord compression and in neoplasia of the CNS.

Normal CSF findings in the face of disease

The CSF shows no detectable abnormality in many cases of disease of the CNS, despite the fact that the CSF may be affected in other animals with the same condition.

The CSF is normal in the majority of cases of:

- Idiopathic epilepsy
- Congenital hydrocephalus
- Functional disorders
- Metabolic disorders
- Intoxications
- Vertebral diseases
- Myelomalacia

This is also true of a significant proportion of cases of:

- FIP
- Distemper encephalitis
- Neoplasia
- GME

Conclusion

Evaluation of CSF is of assistance in confirming the presence of CNS disease in a significant number of patients. However, its value is limited in many cases, as it infrequently provides conclusive information when attempting to distinguish between different causes of neurological dysfunction. It is positively diagnostic in certain circumstances: finding pus cells or organisms in severe infectious processes, finding pleocytosis or increased globulins in inflammatory disorders and the rare findings of neoplastic cells or of globoid cells. In many functional, metabolic and degenerative disorders, there will be no changes in the CSF. Changes in CSF may be poorly correlated with the type and severity of the lesion, although meningeal lesions have particularly marked effects on CSF composition. Some thoracolumbar and lumbar spinal cord lesions may result in changes in the lumbar CSF, but cerebellomedullary samples remain normal (Thomson, Kornegay and Stevens 1990). History, clinical examination and detailed neurological examination are the essential elements in reaching a diagnosis of nervous system disease. CSF examination is a useful adjunct to the interpretation of these evaluations, but rarely is diagnostic *per se*.

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CHAPTER FOUR - Part Two

Electromyography and Nerve Conduction Studies

Ian D. Duncan

INTRODUCTION

The application of electrophysiological diagnostic techniques has become a cornerstone in the investigation of neuromuscular disease in small animals (Griffiths and Duncan 1974, 1978; vanNes 1986). Two principle electrodiagnostic techniques, which utilise the same equipment - the electromyograph (EMG) - are performed. These are: **electromyography**, the investigation of the electrical activity of muscle, and measurement of **nerve conduction**.

These techniques examine the integrity of the motor unit, the basic anatomical and physiological component of the neuromuscular system and the peripheral portion of sensory nerve fibres.

The motor unit consists of the lower motor neuron (the motor fibre and its cell of origin which is found in the ventral horn of the spinal cord and in certain cranial nerve nuclei) and the muscle fibres that it innervates.

Equipment

The expense of EMG equipment has limited its use in the past to veterinary schools and large institutions.

More recently less expensive and second hand EMGs have become available, and this has led to the acquisition of EMGs by certain specialist practices.

The EMG essentially consists of an amplifier, oscilloscope screen and loudspeaker, with a stimulating unit to allow the performance of nerve conduction studies (Bowen 1978).

If more refined sensory nerve testing is to be performed, a signal averaging unit is required to filter out the background noise that is present at the high amplifications required to record sensory action potentials.

Concentric needle electrodes are used to record EMG activity and a ground electrode must be used. For motor nerve conduction studies, two needle electrodes are used to stimulate the nerve and two similar electrodes to record the compound evoked muscle action potential (CEMAP).

Electromyography

There are two parts to this examination, the evaluation of voluntary muscle activity and the testing for spontaneous activity in the resting muscle.

Voluntary activity

Voluntary activity is the electrical activity recorded in a muscle as it contracts, which is brought about by the firing of individual motor units. The individual motor unit potentials (MPs) can be identified on the oscilloscope screen during minimal muscle contraction. The amplitude and duration of these MPs are important parameters, which are measured and compared with control values. As contraction increases, so the number of motor units and their frequency of firing increases, a phenomenon known as recruitment. Eventually, individual motor units become indistinguishable on the oscilloscope screen and this combined electrical activity constitutes the interference pattern. Voluntary activity is difficult to evaluate in small animals. It is possible to examine individual MPs and the interference pattern by inserting concentric needle electrodes into extensor or flexor muscles, with the animal standing or while inducing a withdrawal reflex. In neuropathies, a loss of nerve fibres leads to a drop out of motor units and an incomplete interference pattern (Griffiths and Duncan 1974). In a totally denervated muscle, no MPs are detectable. Conversely, in a muscle which has been re-innervated, the motor units are often enlarged and so the MPs are of a higher amplitude and longer duration.

Spontaneous activity

Spontaneous activity only can be accurately assessed in the anaesthetised animal. It consists of a variety of abnormal potentials, which signify denervation of the muscle or a primary muscle disease. In the normal resting or anaesthetised state, no electrical activity is found, with two exceptions:

- **Insertion activity** is a short burst of activity which corresponds to the mechanical depolarisation of muscle fibres caused by the EMG electrode as it passes through the muscle.
- **End plate noise** is recorded within the area of the neuromuscular junction.

In denervated muscle, the insertion activity may be prolonged and is followed by abnormal potentials, most often fibrillations and positive sharp waves.

Fibrillations are brief, spontaneous potentials which have a low amplitude (20-200 μV) and short duration (1-5 msec). On the loudspeaker, they are described as sounding like cellophane paper being wrinkled or like eggs frying. They arise from single muscle fibres and are triggered by needle movement, which frequently induces a rapid discharge of fibrillations.

Positive sharp waves have a saw toothed shape, a similar amplitude to fibrillations but are of a slightly longer duration. They also are triggered by needle movement and can occur in bursts at high frequency. Both fibrillations and positive sharp waves can be found in certain myopathies, for example, polymyositis, but they are most often signs of denervation.

High frequency discharges, often of positive sharp waves, can be seen in neuropathies.

Fasciculations represent the contraction of a single motor unit. They result from irritant lesions of ventral horn cells (for example, in canine spinal muscular atrophy) or in nerve root lesions (for example, in some cervical intervertebral disc herniations). They fire randomly and appear similar to MPs. Fasciculation may be visible in the animal as small rippling movements on the muscle surface. Myotonic discharges are high frequency bursts of activity which wax and wane in frequency and amplitude, giving them the characteristic sound of a motor bike "revving up". They are induced by needle insertion or movement and by percussion of the muscle, although they can occur spontaneously. They are classically seen in myotonic disorders such as myotonia congenita in the dog (Duncan and Griffiths 1986). High frequency discharges which have a sudden onset and termination and that do not wax and wane are called high frequency repetitive discharges. They often are found in dogs with myopathy associated with Cushing's disease (Duncan and Griffiths 1986).

Nerve Conduction Studies

Techniques are available to measure conduction in both motor and sensory nerves.

Motor nerve conduction

To record from motor nerve fibres, a mixed nerve (containing both motor and sensory fibres) is stimulated at proximal and distal sites. The CEMAP which results from this stimulation is recorded from a muscle innervated by the nerve. For example, in the pelvic limb, the sciatic nerve is stimulated at the greater trochanter and the tibial branch stimulated at the hock. The CEMAP is recorded from the interosseous muscles of the foot. By measuring the latencies from the two sites of stimulation and the distance between the stimulating electrodes, the nerve conduction velocity is calculated. The velocity is a representation of speed of conduction only along the fastest firing fibres. The amplitude, duration and shape of the CEMAP are recorded and reflect the number of fibres firing. A similar technique is employed in the thoracic limb using the ulnar nerve.

Sensory nerve conduction

To measure sensory nerve conduction, a suitable sensory nerve is stimulated distally and a recording of the action potential made directly from the nerve proximally. In the thoracic limb, the lateral cutaneous radial nerve is used. The stimulation site is the digital branch on the dorsum of the foot and the recording made from the nerve in the mid-antebrachium where it runs close to the cephalic vein. The nerve conduction velocity is calculated from the distance between the sites and the latency. The amplitude, shape and duration of the action potential are also recorded.

Effect of neuropathy

The nerve conduction velocity and evoked muscle action potentials are affected both by demyelination and axonal degeneration. In demyelination, NCV is slowed due to lack of the insulating sheath around the axon and loss of saltatory conduction. The CEMAP is no longer bi- or triphasic, but has many phases; the phenomenon of temporal dispersion. As demyelination progresses, nerve conduction will be blocked in certain fibres and the CEMAP will be reduced in amplitude. In axonal degeneration, affected nerve fibres cannot conduct, so the CEMAP is reduced in size as there are fewer intact motor units. However, the NCV will remain approximately normal as long as some large diameter fibres are intact. If the nerve is sectioned completely, it will continue to conduct at a normal velocity distal to the lesion for up to eight days, although the CEMAP gradually declines until the nerve no longer conducts. In sensory nerves, demyelination and degeneration have the same general effect. These techniques only measure conduction in the mid and distal limb. To measure more proximal conduction, late waves are measured, in particular the F-wave and H-reflex (van Nes 1986). These measure conduction through the ventral nerve root and the dorsal and ventral root respectively. They are of considerable use in evaluating lesions involving the nerve roots, for example, polyradiculoneuritis. To test the integrity of the neuromuscular junction, repetitive nerve stimulation of the motor nerves mentioned above can be used. The response to low frequency stimulation (3-5 Hz) is measured. In a healthy animal, this technique leads to a uniform amplitude of the CEMAP. In patients with myasthenia gravis, the CEMAP de-

creases to a lower amplitude after two or three stimuli. This decrement can be quantified.

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CHAPTER FOUR - Part Three

Urodynamic Studies

Jody Gookin and Nicholas J. H. Sharp

INTRODUCTION

Urodynamic studies comprise two basic techniques, the cystometrogram (CMG) and the urethral pressure profile (UPP). Although these are very valuable objective means of assessing micturition, it should be stressed that less objective, but clinically very useful information can be obtained from the neurological examination (see Chapter 12). Conscious control of micturition, the anal reflex, and perineal sensation together assess the sacral spinal cord segments and their integration with higher centres. In particular, the ability to pass a steady stream of urine, with low residual volume, indicates normal detrusor function and should correlate to a normal CMG. Likewise, the ability to retain urine normally without leakage implies a functional urethral sphincter mechanism and should correlate to a normal UPP.

Cystometrogram

This measures intra-vesicular pressure during an induced detrusor reflex. The CMG therefore provides information on threshold volume and pressure, bladder capacity and compliance of the bladder wall.

Sedation

Almost 50% of animals will tolerate a CMG without sedation. When required, xylazine is the sedative of choice, because it consistently causes the least interference with the detrusor reflex. The drug overcomes both voluntary inhibition of micturition and any movement caused by the sensation of bladder distension, but its effect usually lasts no more than 45 minutes. The recommended dose of 1.1 mg/kg IV or 2.2 mg/kg SC often causes bradycardia (with up to a 60% drop in heart rate), cardiac arrhythmias and a fall in cardiac output. Atropine can be used to overcome the deleterious effects of xylazine, but itself has a dose-dependent effect on the detrusor reflex. At 0.06 mg/kg SC, it should have no effect, whereas a higher dose or intravenous administration can cause some interference. Although this subcutaneous dose has been shown not to affect CMG in young healthy dogs, this may not be the case in older patients or those with neurological dysfunction. For this reason, we recommend that atropine not be used during CMG if possible.

If xylazine is contraindicated in an individual dog, acepromazine and oxymorphone (0.11 mg/kg of each IV) can be used, but are less effective in abolishing movement artefacts and may be more suppressive to the detrusor reflex. Diazepam and ketamine do not provide adequate restraint and their use is also associated with considerable artefact.

Method

Following sedation, a suitable sized catheter is placed into the empty bladder and connected via a 4-way valve to a pressure transducer with a strip chart recorder and an infusion pump.

The bladder can either be filled with air or CO_2, or sterile saline by the infusion pump. As filling occurs, intravesicular pressure is measured simultaneously on the strip chart recorder. A Foley catheter with bulb inflated is necessary in the female. The largest sized regular catheter should be used in male dogs and in cats. The tip of the penis may need to be pinched off around the catheter to prevent leakage of fluid and resultant loss of pressure. As an alternative to urethral catheterisation, a percutaneously placed transabdominal catheter has been employed for bladder infusion. This eliminates both outflow resistance and alterations in external urethral sphincter activity caused by urethral catheterisation.

The start of the CMG is characterised by a small initial peak in pressure associated with the initial clearing of fluid within the urethral catheter. A normal bladder with intact innervation then responds to the increase in intravesicular volume with only a minimal rise in pressure (usually less than 20 cm H_2O). Beta adrenergic stimulation is largely responsible for this by causing relaxation of the detrusor smooth muscle. At the threshold pressure / volume relationship (equal to a capacity of approximately 20 ml/kg), the bladder is no longer able to accommodate the increase in volume and a detrusor reflex is initiated. The normal pressure peak is around 70-80 cm H_2O and the catheter should be disconnected 1-2 seconds after this peak as a sustained increase in bladder pressure can cause damage. If no detrusor reflex is observed, the pressure

should not be allowed to exceed 40 cm H_2O (roughly equal to 35 ml/kg). Rarely are such pressures necessary to elicit a detrusor reflex.

For some reason, the first CMG often fails to induce a detrusor reflex whereas a second will succeed. Therefore it is advisable to perform at least two tests during each evaluation period. The major reasons for failure to obtain an adequate study are:

- excessive artefact resulting from inadequate sedation
- conscious inhibition of the detrusor reflex
- pharmacological depression of the detrusor reflex.

The most commonly recognised abnormalities are:

- capacity and threshold can be reduced by bladder fibrosis
- the pressure peak can be lowered by sacral spinal cord or nerve root lesions
- decreased compliance can be caused either by bladder wall fibrosis, or by inference with beta sympathetic control of smooth muscle relaxation.
- lowering of the pressure peak can also be caused by leakage around the urethral catheter.

A normal CMG trace is shown in Figure 4.3. If an EMG needle is inserted into the external anal sphincter during CMG, the co-ordination of the detrusor and external urethral sphincter can be recorded. This is because the external anal sphincter contracts synchronously with the striated external urethral sphincter (urethralis muscle).

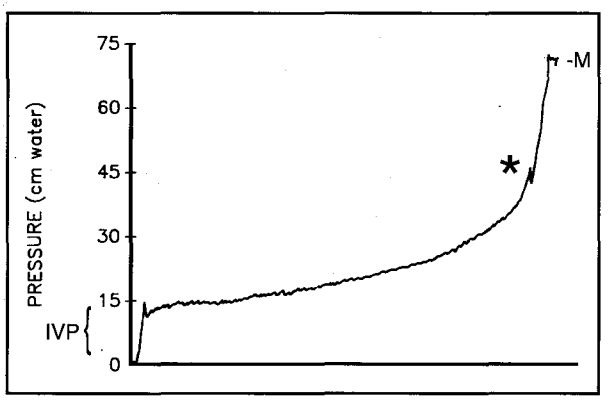

Figure 4.3: *Normal cystometrogram (CMG) trace. Intravesicular pressure is indicated by IVP; threshold volume/pressure relationship for this dog is indicated by the asterisk; and maximal contraction pressure by M.*

Urethral Pressure Profile

Urinary continence has been described as a condition in which intra-urethral pressure exceeds intra-vesicular pressure. The UPP measures intra-urethral pressure as a recording (urinary) catheter is pulled distally from the bladder, into and along the urethra. The resting urethral pressure is derived from three components:

1. Connective tissue and vascular tone of the urethra.
2. The urethralis skeletal muscle, under pudendal nerve control, located just distal to the prostate in males and just distal to the urethral midpoint in females.
3. The urethral smooth muscle, under adrenergic sympathetic control, provides the most important contribution.

Thus, it can be seen that there is no specific anatomical urethral sphincter, but rather a combination of structures which together result in a sphincter mechanism.

Sedation

We prefer to use no sedation if possible to perform the UPP. As some animals will tolerate a CMG without sedation, we usually attempt a CMG prior to the UPP, which eliminates the need to catheterise the patient twice. If this is not successful, the UPP is attempted without sedation and then the CMG is performed after sedation.

A wide array of sedatives have been used for the UPP, although all have been associated with significant reductions in UPP parameters. Xylazine (1.1 mg/kg IV or 2.2 mg/kg SC) is commonly employed to sedate dogs for UPP since it is the drug most often used for CMG. The results of its sympatholytic effect on urethral smooth muscle tone and depression of the urethralis muscle external sphincter are shown by the dotted lines in Figures 4.4 and 4.5. The addition of atropine to normalise the cardiovascular effects of xylazine does not further affect the UPP.

Recently, propofol (6.5 mg/kg IV induction, 0.25 - 0.50 mg/kg/min maintenance) has been shown to have less of a depressive effect on the UPP. These findings suggest that it will be a useful alternative to xylazine in animals requiring sedation (Table 4.2). Appropriate reference values need to be utilised for each drug.

Method

Two different techniques have been employed to measure urethral pressure, namely the perfusion and the microtransducer methods.

The perfusion method employs a suitably sized (usually 8 french) urethral catheter with a single side hole. The catheter is connected via a 4-way valve to the same pressure transducer, strip chart recorder and infusion pump as are used for CMG. The exposed portion of the catheter is held in a special withdrawing device in order to slowly pull the catheter tip from the bladder along and out of the distal end of the urethra. As the tip is withdrawn, the transducer simultaneously records the pressure at the catheter side hole. This pressure is generated by the response of the urethra to the distension caused by a simultaneous slow steady infusion (such as 2 ml/min) of sterile saline into the

Table 4.2: UPP values in healthy dogs and cats before and after sedation.

Medication	MUP cm H_2O	MUCP cm H_2O	FPL cm	Ref.
Intact female dogs				
None	90.18 ± 4.48	79.72 ± 4.61	8.68 ± 0.57	2
Xylazine	-	23.3 ± 7.6	5.4 ± 0.9	1
	33.0 ± 4.54	23.0 ± 4.54	6.23 ± 0.98	2
	36.8 ± 17.0	32.5 ± 16.0	7.2 ± 1.9	3
	26.0 ± 9.0	18.0 ± 5.0	5.1 ± 0.9	4
Xylazine + Atropine	22.0 ± 8.0	15.0 ± 8.0	5.1 ± 0.9	4
Propofol	-	51.0 ± 7.4	6.6 ± 1.7	1
Intact male dogs				
None	109.77 ± 11.52	99.77 ± 11.71	24.0 ± 0.92	2
Xylazine	52.38 ± 6.0	41.77 ± 6.10	19.19 ± 1.94	2
Intact female cats				
Xylazine	76.6 ± 26.7	71.4 ± 25.0	4.4 ± 1.5	5
Intact male cats				
Xylazine	163.2 ± 47.5	161.6 ± 47.1	10.53 ± 0.53	6

1 - COMBRISSON *et al* (1993)
2 - RICHTER and LING (1985)
3 - ROSIN *et al* (1988)
4 - BARSANTI *et al* (1980)
5 - GREGORY and WILLITS (1986)
6 - GREGORY *et al* (1984)

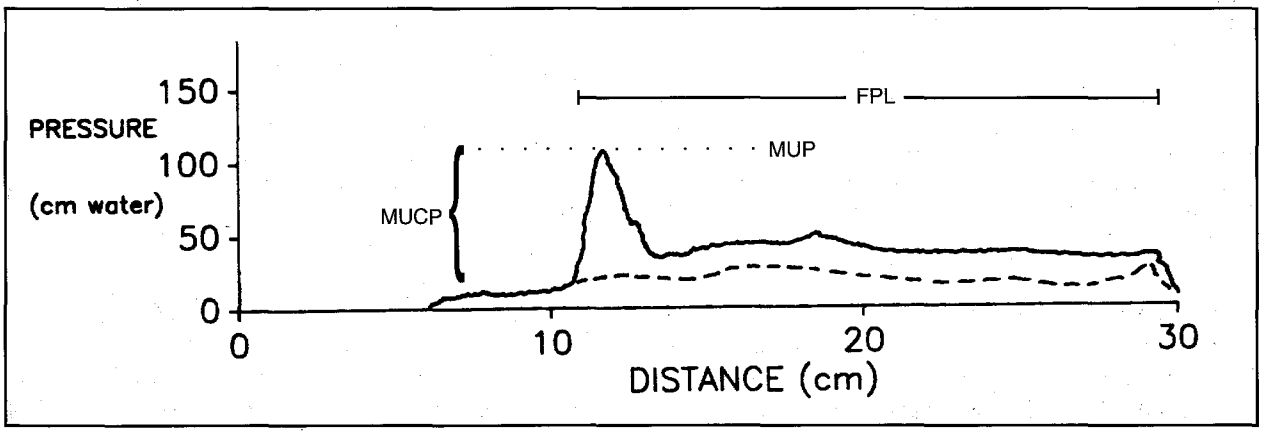

Figure 4.4: *Diagram to show normal canine urethral pressure profile. Values obtained without xylazine - solid line; values obtained with xylazine - dotted line. MUP is the maximal urethral pressure; MUCP is the maximal urethral closure pressure; FPL is the functional profile length.*

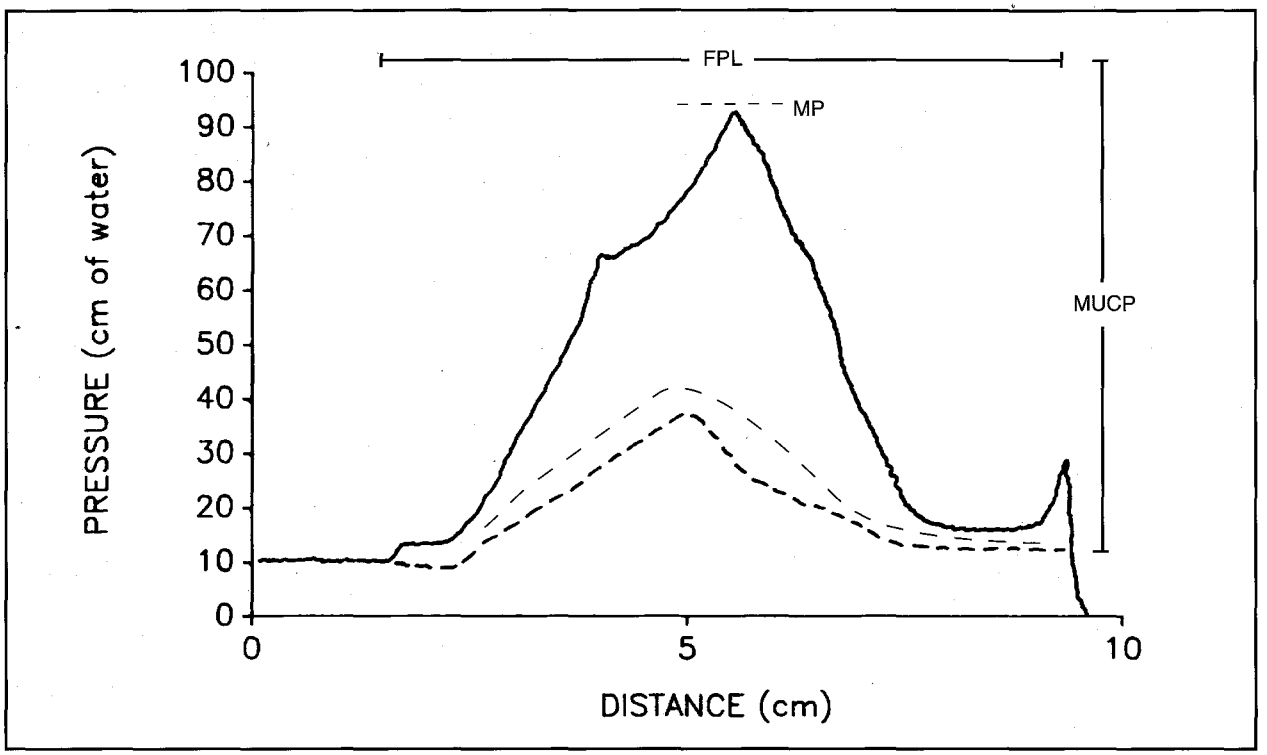

Figure 4.5: *Diagram to show normal female canine urethral pressure profile. Values obtained without xylazine - solid line; values obtained with xylazine - dash line; with propofol - long dashes. MP is the maximal urethral prssure; MUCP is the maximal urethral closure pressure; FPL is the functional profile length.*

catheter from the infusion pump. The catheter withdrawal rate should be the same as the chart speed, in order to allow correlation of events on the pressure trace to their exact anatomical locations along the urethral length.

The microtransducer method does not depend on the mechanical transmission of pressure along the catheter because pressure is measured directly at the catheter tip where it is generated. It is also able to simultaneously measure intra-vesicular and urethral pressures, as a control for variations in intra-abdominal pressure. Drawbacks to this method are the need for general anaesthesia and for the microtransducer itself.

To eliminate sources of error in UPP determination, the following recommendations can be made:

- Air bubbles in the perfusion system will damp the pressure trace and should be avoided.
- The withdrawal apparatus should not allow the catheter to rotate. A rod-driven apparatus causes less artefact.
- Positioning in right lateral recumbency with the transducer oriented dorsally causes least variability.
- For the perfusion method the bladder should initially be empty and the pressure transducer should be calibrated at the level of the urethra.
- A catheter withdrawal rate of 1 mm/sec or less should be used with microtransducers, as high rates can artificially lower readings.

Normal dog and bitch UPP's are shown in Figures 4.4 and 4.5. The following measurements can be obtained:

- Maximal urethral pressure (MP) - the highest pressure in the profile, which correlates with the location of the skeletal muscle sphincter in both sexes.
- Maximum urethral closure pressure (MUCP)- the difference between the MP and intra-vesicular pressure. This has the closest relationship to continence.
- Functional profile length (FPL) - the length of urethra over which the pressure exceeds that within the bladder.

In males, there is often a small pressure peak at the tip of the penis due to engorgement of the glans during catheter withdrawal. If the catheter is fitted at the tip with small bipolar recording electrodes, the location of the urethralis muscle can be identified by its resting electrical activity. When displayed alongside the UPP trace, EMG activity should be coincident with the MP.

Incontinent animals have a shorter FPL and lower MUCP than those which are continent. The MP may decline with age in bitches.

The UPP only measures resting urethral tone, which is good for investigating urine leakage that occurs during the storage phase such as a deficient urethral closure mechanism, or for partial obstructions of the urethra such as a urethral mass or a stricture.

The UPP can provide objective data on alterations in urethral tone, and has therefore proven to be a useful tool for evaluating pharmacological (see Chapter 12) and surgical manipulation of urethral function. It has been used to show that colposuspension results in increased proximal urethral pressures. The UPP is of less value for dynamic problems occurring during the voiding phase, for which uroflowmetry is more useful.

Complications

Up to 2% of CMG's in humans result in urinary tract infection (UTI). These probably result from distension of the bladder, which increases its susceptibility to infection by bacteria introduced with the catheter. Catheterisation without distension (e.g. UPP) is not associated with the same infection rate. In one study, nine out of twenty dogs developed UTI following CMG. Scrupulous attention to sterile technique and routine cleaning of the tip of the penis with betadine are important. A single dose of intravenous antibiotic just prior to the procedure should be considered. Haematuria is another common result of the distension produced during CMG and was seen either grossly or microscopically in twelve of the same twenty dogs. In another study, pain and macroscopic haematuria were consistently seen if intravesicular pressure was allowed to exceed 40 cm H_2O.

Urodynamics in the Cat

In the cat, xylazine (1.1 mg/kg IV) is necessary to perform a UPP or CMG. The MUP tends to be at the distal urethra in the queen and the post-prostatic urethra in the male cat, which correlates to the location of the striated muscle sphincter. No difference in MUP is found between spayed and entire females or between male cats undergoing minimal and maximal dissection perineal urethrostomy. It has been shown experimentally that phenoxybenzamine (0.5 mg/kg), acepromazine (0.1 mg/kg), dantrolen (1 mg/kg) and diazepam (0.5 mg/kg) are effective in decreasing the urethral pressure.

Other Techniques

Electromyelography is an evaluation of the bulbospongiosus reflex. Stimulation of sensory nerves in the bladder wall via electrodes placed in the tip of a urinary catheter is performed while recording events in the external anal sphincter muscle (which contracts synchronously with the urethralis muscle). This checks the integrity of pelvic and pudendal nerves, as well as the sacral spinal cord segments.

Uroflowmetry measures urine flow and, therefore, urethral function during the emptying phase of micturition rather than the static state assessed by the UPP (Richter 1989).

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CHAPTER FOUR - Part Four

Nerve and Muscle Biopsy

Simon J. Wheeler

INTRODUCTION

Both the peripheral nervous system and the musculature of animals are amenable to biopsy in many situations, but careful consideration is required before performing these procedures. It is not adequate to remove a piece of tissue, either surgically or otherwise, place it in formalin and submit it to a diagnostic laboratory.

Such specimens are most unlikely to provide diagnostic information and the procedure may well have a detrimental effect on the patient. Thus, careful planning of the procedure, correct handling and fixation of the tissue, and expert interpretation are all required in performing a biopsy.

Nerve Biopsy

The general principles regarding nerve biopsy have been reviewed by Dyck *et al* (1984) and apply to animals as much as humans.

Whilst the examination of a biopsy is useful in selected cases of peripheral neuropathy, it is not a procedure that should be performed in all patients. It should probably be performed by clinicians with a special interest in the subject who have access to the correct processing methods and who can interpret the findings.

The indications for nerve biopsy are patients where the presence of a neuropathy has been confirmed by clinical and electrophysiological testing, and where further information regarding the nature of the neuropathy is desired.

Nerve biopsy should not be performed where neurological dysfunction is considered to be a possibility, but no other tests have been performed to confirm this.

Biopsy of nerve will lead to the development of neurological deficits and possibly have painful sequelae; this must be remembered prior to performing the procedure, which is done under general anaesthesia.

Peripheral nerve may be collected from a number of sites in the body, the appropriate one being determined by the neurological findings and the results of electrophysiological testing.

The following are suitable sites for biopsy:

- Sensory nerves: Lateral cutaneous radial, Medial cutaneous radial, Saphenous, Superficial peroneal
- Mixed nerves: Ulnar (at elbow), Tibial (above hock)
- Nerve root: Cranial lumbar
- Plexus: Brachial

In collecting a biopsy of sensory nerves, it is possible to remove the entire thickness of nerve and similarly, in the cranial lumbar region (L_1-L_3), a whole nerve root may be harvested. Where a mixed nerve or plexal nerve are being collected, only a fascicle may be removed.

The nerve is approached and isolated, with great care being taken to avoid handling the nerve. The nerve or fascicle is sectioned at the proximal end, and a 2-3 cm portion dissected free with either sharp pointed scissors or a No. 11 scalpel blade. The distal end is cut free and the nerve removed. The portion of nerve should only be held by the ends, not by the middle portion. The nerve must be maintained in its longitudinal orientation during fixation, this being most easily achieved by placing it on a piece of dry filter paper or card. Some method of denoting which end of the nerve is proximal is useful. The biopsy is fixed in phosphate buffered glutaraldehyde.

Processing of the biopsy involves the preparation of semi-thin and thin sections for light and electron microscopic examination respectively. A portion of the nerve is retained for single fibre teasing and subsequent examination. Details of the histological methods are given by Dyck *et al* (1984).

Evaluation of the nerve requires a qualitative appreciation of the structure and any pathological change in both the sections and the teased fibres and a quantitative analysis of the fibre composition and of internodal length. Using these methods, comparisons may be made between normal, age matched individuals and the patient (See Braund 1994).

Muscle Biopsy

Muscle biopsy is also readily performed, but similar considerations apply here as in nerve biopsy. There should be good supportive evidence of myopathy before a biopsy is collected. In selecting a muscle to sample, it is wise to choose one that is neither free from the disease process or one which is most severely affected. The triceps, biceps femoris and cranial tibial muscles are most frequently selected. If motor end plates or terminal nerve branches are to be examined, the lateral digital extensor muscle may be removed intact and the area where the intramuscular nerves enter then processed for examination.

The muscle to be sampled is exposed surgically and the direction of the muscle fibres identified. It is necessary to maintain the muscle sample in its longitudinal orientation following removal. This is achieved by applying a muscle clamp to the fibres and dissecting the portion of muscle free around this clamp. This ensures that the piece of muscle to be evaluated is not damaged and that contraction artefacts are avoided. The muscle section, still in the clamps, is frozen in liquid nitrogen. Other portions of muscle are immersed in glutaraldehyde for electron microscopy and in formalin.

Processing of the muscle involves preparation of sections for light and electron microscopy. Also, the frozen muscle is stained histochemically to allow muscle fibre type identification and subsequent morphometric evaluation. Biochemical analysis of the frozen muscle may also be undertaken (Swash and Schwartz 1981; Kakulas and Adams 1985). If motor point evaluation is to be made, the muscle is stained with methylene blue.

The collection, processing and evaluation of muscle and nerve material by biopsy requires careful planning and expertise. The relatively non-specific collection of samples fixed in formalin is unlikely to prove diagnostic and may be detrimental to the patient. These procedures should probably be restricted to situations where suitable expertise is available.

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CHAPTER FIVE

Neuroradiology

Jeremy V. Davies

INTRODUCTION

This section is devoted to the equipment and techniques involved in creating images of the axial skeleton, the relevant radiographic anatomy, and the radiological recognition of conditions affecting the nervous system. Some special techniques relevant to neurological disease are also discussed and advanced imaging modalities explained. Whilst examples are given of the commonly encountered neurological conditions, the reader will be encouraged to adopt a systematic approach to the evaluation of radiographs and other images. Changes in the image can be considered as indicators of possible pathological change. Certain physiological and pathological processes will change the appearance of the image in certain ways. Those changes can be analysed to formulate a possible diagnosis. The fundamental changes in radiographic appearance are sometimes known as **Roentgen signs.**

GENERAL UNIVERSAL DESCRIPTION OF RADIOPATHOLOGICAL CHANGE (ROENTGEN SIGNS)

Radiographic changes can be classified in almost all instances in the following way:-

Changes in:-

- Position
- Size
- Number
- Opacity
- Contour or margin
- Internal architecture
- Function

In the light of these changes, the type of pathological process can be determined and a probable list of differential diagnoses offered.

IMAGING EQUIPMENT

Conventional Radiography

Radiography of the head and spine should always be carried out under general anaesthesia so that accurately positioned images can be obtained. The complex anatomy of these structures is rendered even more difficult to appreciate if the images are rotated or oblique. On rare occasions, for example, following severe trauma when cranial or spinal fractures / dislocations are suspected, conscious survey films may be taken. In such cases, gross lesions are expected and accurate positioning is less important. There is also the possibility that manipulation of the anaesthetised and therefore unsupported body could exacerbate injuries. Any natural resistance that the patient offers may be an indication of the location and severity of the problem. An example of this would be the suspected atlantoaxial subluxation case. Flexed views of the neck will exaggerate the radiographic appearance of the dislocation but could, at the same time, seriously compromise the spinal cord. Gently flexing the neck in the conscious dog can produce satisfactory images, and at the point at which flexion may be potentially hazardous, the dog will tend to offer some resistance.

When general anaesthesia is employed, long exposure times do not create a significant problem as the patient will be still. The only area of difficulty might be the thoracic spine, where respiratory movements could cause movement blur. This can be overcome by freezing respiration temporarily, by closing the anaesthetic circuit and compressing the rebreathing bag. (Such procedures must be carried out with due attention to radiation safety of personnel.) It is therefore possible to obtain images of the skull and spine of all but the very largest dogs using relatively low output equipment. Ideally, equipment with a capability of at least 100mA and 100kV should be available. All areas of interest that are greater than 10cm in depth should be radiographed using a grid. This will require higher exposure factors, but will produce a higher quality image. In order to facilitate interpretation and to maximise image quality, severe beam collimation should be employed, and to this end a light beam collimator is essential.

Modern fast film / screen combinations using rare earth phosphors provide high detail images whilst minimising the exposures required. Recently, ultraviolet emitting phosphors have been introduced. These are comparable with both green and blue emitting

phosphors. Very high detail single emulsion systems such as those used in mammography can produce exquisite detail of bony architecture if the integrity of vertebrae requires detailed examination. Such images will often show subtle mineralising changes in the intervertebral discs, which may not be appreciable with regular film / screen combinations.

A Bucky couch is ideal so that accurate positioning can be carried out without the patient having to be positioned on the cassette and grid, which tends to cause deformation of the patient with respect to the beam. Tilting couches are advantageous for myelographic procedures, especially when very large breeds require tilting to assist the flow of contrast in the thecal sac. Tables that tilt in both directions are helpful so that a bolus of contrast can be encouraged to move in either a cranial or caudal direction if required.

Linear Tomography

Tomography utilises motion as a means of "highlighting" some part of the patient to produce a "slice" image. It is possible to move the X-ray tube, the patient or the image receptor. To create the tomographic effect two of the three elements are moved. In most systems the X-ray tube and image receptor are moved. It is essential that the movements are synchronised and coordinated with the exposure control. The simplest form of tomography is linear tomography. The X-ray tube and image receptor move in opposite directions about a fulcrum. The height of the fulcrum above the table can be adjusted as can the arc of travel (usually about 15°, but can be as much as 30°) (Figure 5.1). All the parts of the patient that lie within the plane of the fulcrum will "not move" and so will appear sharp. All parts below and above the plane will be blurred by movement. The wider the arc, the thinner the slice. The image is then viewed as any other radiograph and to the untutored eye looks like a terrible film with much blurring (Figure 5.2).

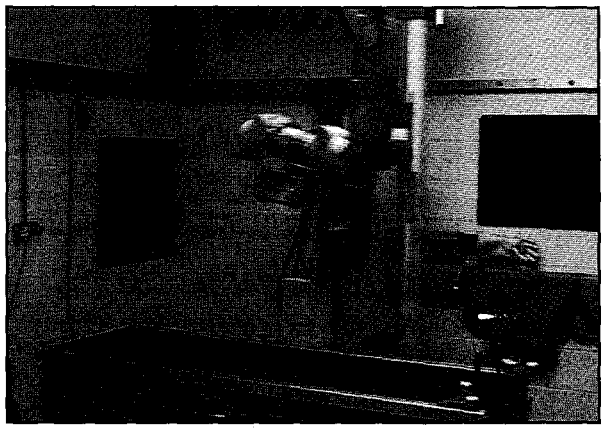


Figure 5.1a: *Linear tomographic set up. Note the tube head is blurred as it is travelling through its arc of motion whilst being photographed. The Bucky tray to which it is attached is out at the moment and is moving in the opposite direction to the tube. The fulcrum is adjusted at the white vertical panel attached to the back of the table underneath the tube.*

Figure 5.1b: *Fulcrum adjustment to set the plane of tomographic cut.*

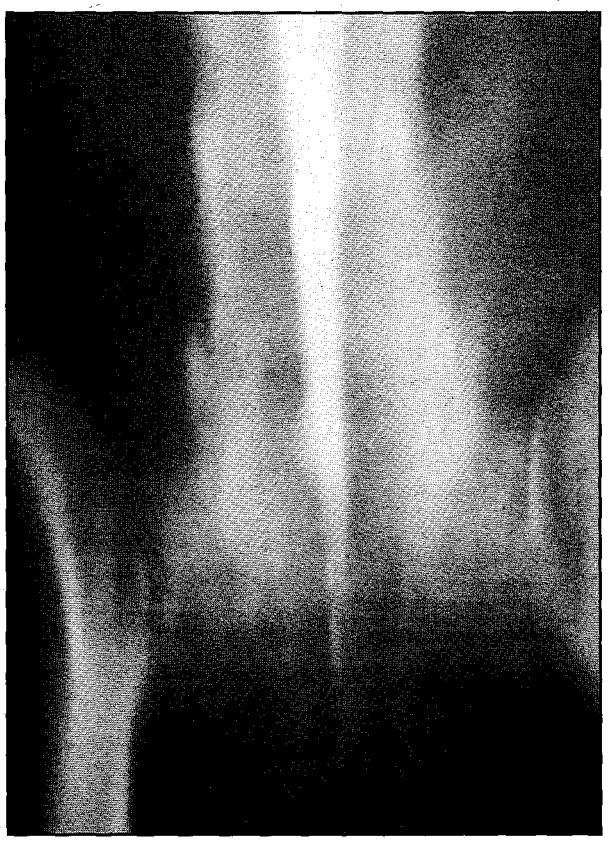


Figure 5.2: *Linear tomogram of the contrast filled thecal sac at the lumbosacral joint. The thecal sac is in the plane of tomographic cut and sharply outlined. The vertebral and pelvic bony shadows are blurred out. Note the outpouching of contrast around a nerve root displaced on the right.*

Other patterns of blurring have been devised for tomography, e.g. curvilinear, circular, trispiral, hypocycloidal etc. Further geometric improvements were devised, but with the explosion of computer technology in the 1970s it became apparent that if the image were captured electronically rather than on film, the oscilloscope image could be digitised and manipulated "mathematically" by the computer. It is this combination of technologies that forms the basis of computed tomography.

Body Scanners - Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)

When CT and MRI investigations are carried out, general anaesthesia poses some practical problems. During each CT slice, exposure radiation is emitted and personnel must leave the room. It is therefore necessary to provide a controlled anaesthetic system that can be checked periodically, or to use a relatively long acting intravenous agent that requires little intervention. In the author's experience intravenous pentobarbitone to a light plane of surgical anaesthesia with an endotracheal tube in place is very effective. Often "head" cases may have seizures as part of their clinical picture, in which case pentobarbitone is eminently suitable. During MRI it is not possible to have "loose" magnetic objects in the imaging room, and again routine anaesthetic apparatus may be impractical and so an intravenous technique is preferred. In most MRI facilities special non-magnetic anaesthetic trolleys will be available, but if these are for human use only the veterinary clinician will have to resort to an intravenous method. Problems arise when CT images of the abdomen and chest are required, where the movement of breathing may spoil the image. In those cases a long circle or coaxial rebreathing system that can be led from the imaging room can be used. Most human CT scanners have built-in recordings telling the patient when to hold their breath. During these times the circle can be closed and the rebreathing bag gently compressed to inflate the lungs, and momentarily freeze respiratory movement.

Computed tomography

There have been four generations of scanner, the major improvement each time being a shortening of the scan time. The first generation scanner had two image receptors that were rotated in harmony and in sequence around the patient. This was, not surprisingly, slow. Now the fourth generation scanners have multiple image receptors and one X-ray tube (Figure 5.3). This has reduced the time of a scan to a few seconds from about five minutes per slice. The computer can then construct slice images in sagittal, transverse or coronal (frontal) planes. If set in one plane, it is possible for the computer to reconstruct a crude image in one of the other planes, or obliquely. This reconstruction is slow and the image poor, but can be directed at an area of special interest. Modern software is improving this facility and can even offer 3D reconstructions. It is also possible to magnify or "target" the image. This can help when the area of interest is small e.g. a cat's skull. The disadvantages of targeting are that the slice construction times are longer, and as with many enlargement techniques the artefacts or "noise" are also magnified.

The matrix of pixels produced by the computer represents the averaged attenuation of the anatomy in a particular voxel. A pixel is a small two-dimensional

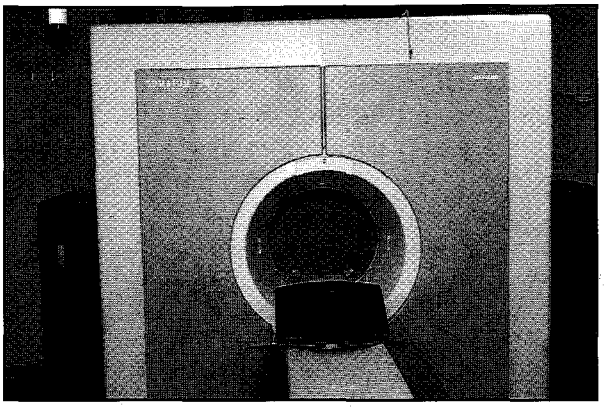


Figure 5.3a: *CT scanning gantry and couch.*

Figure 5.3b: *A retriever within the CT tunnel for a head scan. Notice the accurate positioning of the skull and the intubation associated with IV pentobarbitone anaesthesia.*

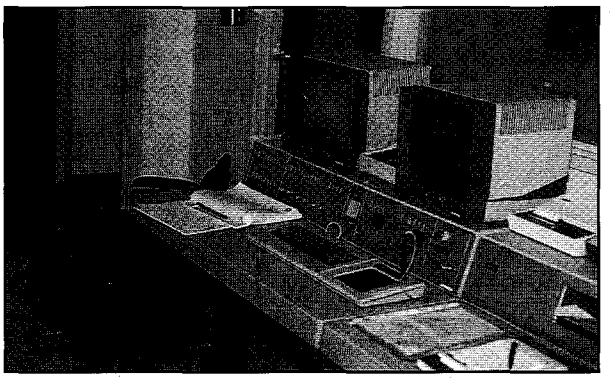


Figure 5.3c: *CT control panel. Because of the radiation hazard, this is outside the scanning room protected by an attenuating wall and a lead glass panel.*

area of image information whereas a voxel is the three-dimensional cube of tissue (pixel x slice thickness) that has attenuated the beam. Slice thickness can be set between 2 mm and 10 mm. Each pixel is assigned a shade of grey. The darkness or lightness of this shade of grey can be manipulated by the computer transforming the overall appearance of the image. The two controls are referred to as the "window" and the "level". The density or attenuating property of the tissue in a voxel will be represented by a number from +1000 to -1000. This scale of CT numbers is called the Hounsfield scale, and particular tissues have predictable CT or Hounsfield numbers e.g. cortical bone +1000, water 0 and air -1000. The display on the oscilloscope will depict +1000 as bright white and -1000 as dense black. The computer can be set to depict a window within the grey scale anywhere between +1000 and -1000. This could be a wide window or a narrow window. Narrow windows provide greatest tissue differentiation, and are used when soft tissues are under investigation. Wide windows provide poorer tissue differentiation and make bony structures stand out relative to all other tissues, and are used when skeletal structures are under scrutiny. They are often referred to as soft tissue windows (50 - 300) or bone windows (2000 +). Adjusting the level sets the central shade of grey at some point in the selected window. Windows and levels are selected at the beginning of the scan for the type of examination being undertaken (Figure 5.4). As these adjustments are a computer exercise and do not influence the radiographic exposure factors, they can be altered during or after the scan to fine tune the image or enhance an area of suspicion.

Image information is stored on computer media (magnetic tape, disc, optical disc) and displayed on an oscilloscope or on hard copy by dry silver imager, multiformat camera or laser camera.

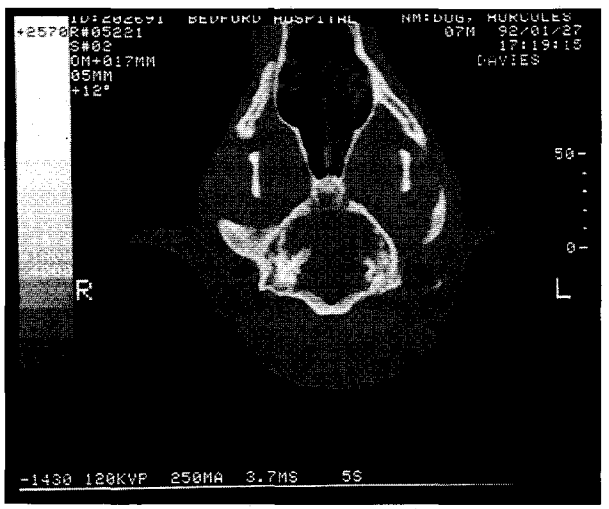


Figure 5.4a: *"Bone window" setting. The window is set at 4000 and the level at +570. This shows the bony structures of the skull and nasal cavity well, but most soft tissues have the same, homogeneous soft tissue opacity. This patient has a left sided sinonasal adenocarcinoma, which can be seen in the caudal nasal chambers on both this and Figure 5.4b.*

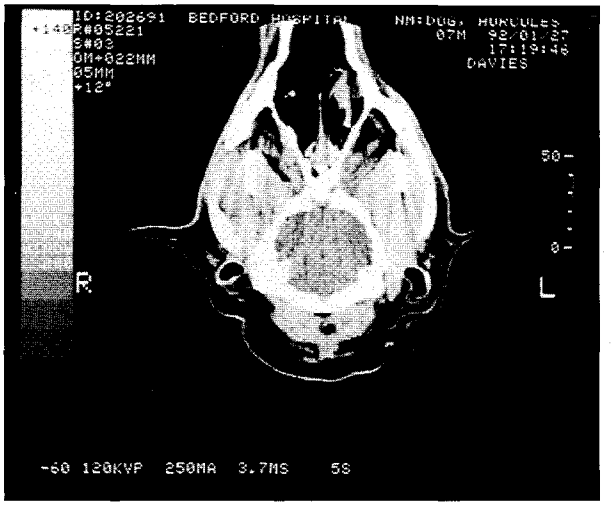


Figure 5.4b: *"Soft tissue window" setting. The window is set at 200 and the level at +40. This setting allows both the intracranial and extracranial soft tissues to be more readily differentiated.*

The ratio of skull bone thickness to brain volume in small animals renders CT images rather coarse with a high level of artefact or "noise". Artefacts often appear as diagonal, parallel, linear, lucent shadows ("streaking") similar to the marks made by a mower on a lawn. Such artefacts can be caused by patient movement. High density anatomy or objects such as orthopaedic implants will have a similar effect. Interfaces between high and low density anatomy can cause an artefact called "beam hardening", where a wide zone of apparently low attenuation is seen. A frequent manifestation of this is in the brain stem at the level of the petrous temporal bones. A more complex artefact that occurs is the so called "partial volume effect". Each pixel (tiny square of image information) viewed on the screen is a representation of a cuboid (voxel) of anatomy that is as long as the slice thickness (2 - 10 mm). All attenuating materials within that voxel will be averaged and a shadow of greater or lesser attenuation than would be expected may be created. This is most likely to occur when the edge of a structure is curved or when the slice incorporates only a thin edge of a larger structure. Careful examination of preceding and succeeding slices at that particular level will allow the viewer to determine whether a shadow is actual or a partial volume artefact.

As the principles of CT are based on the physics of X-radiation, the images collected have the same radiological features as a conventional radiograph. Bone is depicted as a white or bright shadow with soft tissue, fluid, fat and air of decreasing opacity. Interpretation is therefore based on conventional radiological principles.

Magnetic resonance imaging

The technique was formerly known as nuclear magnetic resonance (NMR) and has been used in physicochemical research for many years. Only relatively

recently has the technique been modified for medical imaging. A similar looking apparatus to a CT scanner is employed, with the fundamental difference being that the energy sources employed to create an image are magnetic fields and radio frequencies rather than X-ray photons (Figure 5.5). The data collected is handled by computer and similar slice images created.

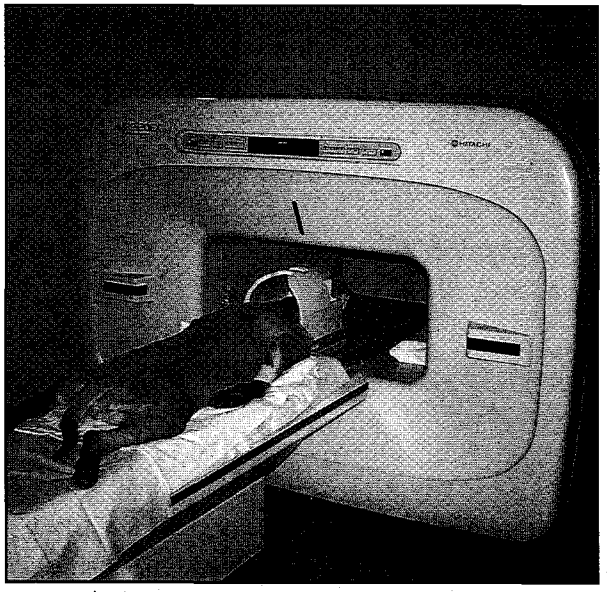


Figure 5.5: MRI scanner. The room is shielded because of the high magnetic field. Magnetic materials - equipment, personal effects, etc. must be left outside.

When the patient occupies the tunnel of the scanner the body is subjected to a very strong magnetic field, which causes all the magnetic components within the body to adopt the same alignment. Hydrogen atoms are especially sensitive to the magnetic field applied to the patient in MRI, and so tissues with high hydrogen content are clearly depicted whilst substances such as bone and air are ignored. The resultant image is a map of the hydrogen nuclei within the body.

The applied magnetic field aligns protons within hydrogen nuclei and causes precession of nuclei. Precession is the cone shape described by the axis of a tilted spinning top. The frequency of this precession is called the Larmor frequency. To create an image the equipment applies a pulsed radio frequency (RF) to the precessing protons and then "listens" to the RF emissions from those protons. This alternating transmission and reception of RF allows the proton map to be constructed.

The MRI process can be controlled by various parameters. Two of these parameters, the longitudinal relaxation time (T1) and the transverse relaxation time (T2), alter the contrast of the image and are frequently referred to as T1-weighted or T2-weighted images. T1 weighted images are dependent on tissue composition, structure and surroundings, and give a more accurate representation of anatomical structure. T2 weighted images depend upon the physical state of a substance and show greater tissue contrast or differentiation. It is usual to collect both types of image during an investigation. MRI is very sensitive at detecting subtle tissue differences as well as tissue chemical states. T1 and T2 images are easily differentiated in brain scans by the appearance of the CSF. On T1-weighted images the CSF is dark (hypointense) and on the T2-weighted images bright (hyperintense). MRI has the advantage of being able to differentiate tissue types, potentially avoiding the need to biopsy lesions.

Tomographic (CT and MRI) Contrast Studies

Brain

When examining the brain with CT, IV contrast enhancement can be used. Water soluble contrast media (WSCM) are administered at a concentration equivalent to 300-400 mg iodine per ml, and at a dose rate of 2ml/kg. Because of the volume and viscosity of the medium, it is best warmed to room temperature and administered via an indwelling catheter in a suitable peripheral vein. Regular ionic WSCM such as Urografin®, Hypaque®, Conray®, etc. can be used. More expensive non-ionic media such as Omnipaque®, Isovist,® Niopam®, and Amipaque® are not necessary, but could be considered in high risk patients such as trauma patients. As is routine with all radiographic contrast studies, a set of plain images should be collected first. Following the injection of the intravenous WSCM, the contrast enhanced slices can be collected immediately. The contrast will deposit itself in or around lesions with increased blood supply thus enhancing certain space occupying lesions. The nature of the enhancement is variable and may contribute to categorising the lesion. Post-contrast enhancement slices can be viewed under the same settings (window and level) as the plain slices, although some centres prefer to increase the contrast slightly following enhancement.

Contrast studies of the brain using MRI require a different contrast medium. Paramagnetic contrast media are said to be T1 active or T2 active. The medium Magnevist® (dimeglumine gadopenteticate–gadolinium) is most often used. The medium is administered intravenously at a dose rate of 0.2 ml/kg by IV bolus injection. Opacification is observed immediately and for about 45 minutes after administration. T1-weighted sequences are preferred.

Spine

If an intravenous study, as described above for the brain is carried out contrast will be visible in vascular compartments for some time after injection. Images of the spine will show contrast in the venous plexuses ventral to the spinal cord. Deviation or compression of these contrast-filled vascular spaces can imply the presence of a space occupying lesion, but this would be a rather erratic technique to employ for routine examination of the vertebral canal.

Conventional myelographic techniques can be employed prior to CT scanning, but because of the sensitivity of the imaging system the opacified CSF can be so enhanced that it obscures other parts of the image. If a CT examination is to be carried out immediately following routine myelography or directly after the administration of intrathecal contrast, then approximately 20% of the dose should be administered and the patient tilted to allow sufficient mixing of the contrast with the CSF for a short time prior to imaging.

Spinal MRI imaging is in its infancy in veterinary radiology but may prove to be the technique of choice in some conditions e.g. lumbosacral disease. The images so obtained could also be enhanced using gadolinium.

Other Imaging Techniques

Other imaging techniques may prove useful in brain disorders.

Scintigraphy may provide information in some patients, but the resolution of this imaging method is rather poor and this limits the usefulness. Despite this lack of specificity, the sensitivity of scintigraphy is high in pathological states where vascular activity is altered (increased or decreased). This reveals areas of increased uptake of radiopharmaceutical ("hot spots") or decreased uptake ("cold spots"). The identification of very early bone lesions such as metastatic neoplasia is particularly appropriate for this imaging modality. SPECT scintigraphy (Single Photon Emission Computed Tomography), a combination of scintigraphy and CT has proved useful in the detection of brain lesions in some circumstances, though veterinary applications have been limited.

More advanced computer software has allowed three-dimensional reconstructions to be made of CT and MRI images. Such images are particularly useful for surgical planning and cosmetic reconstructive techniques in man.

The fundamental principle of MRI that maps proton density has been harnessed to provide vascular images. In such techniques the apparatus is programmed to map moving precessing protons i.e. those within the blood circulating in the vasculature. These techniques are termed vascular MRI (VMRI) or MR angiography (MRA), and provide exquisite images without the need for catheterisation techniques or contrast media.

Other areas of imaging development include MR spectroscopy (MRS) and positron emission tomography (PET).

Ultrasonography is almost excluded in neuroimaging because of the bony case surrounding the brain and spinal cord. It is possible to image the brain via open fontanelles and in man images can be obtained through very thin bony plates. The relative thickness of domestic animal skulls renders this an unlikely area of development.

RADIOGRAPHY AND RADIOLOGY

HEAD (CRANIAL VAULT, CALVARIUM)

Techniques

The anatomy of the calvarium is complex and breed variations diverse. Fortunately, the number of recognised conditions is small and their complexity minimal. However, it is essential to achieve accurately positioned radiographs as even small degrees of misalignment may lead to erroneous interpretation.

The availability of tomographic slice images from CT and MRI has revolutionised imaging of the skull and its contents. It must not be overlooked that accurate positioning for these techniques is equally important. Tomographic slice anatomy can cause difficulty in orientation at first, but with experience is quite straightforward. Certainly, the fact that most axial anatomy is bilaterally symmetrical, and slice views show both sides of the axis, renders comparison of normal with abnormal within the individual simple. In order for this comparison to be made it is imperative that positioning is consistent and accurate.

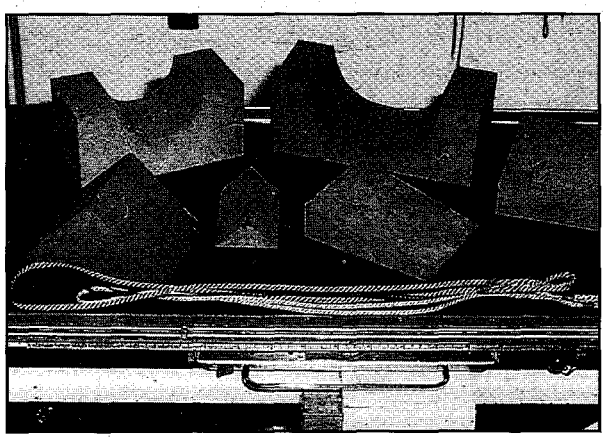


Figure 5.6: Useful positioning aids:- lucent foam shapes, ties (football boot laces, calving ropes), floppy sandbags (must not be overfilled).

In all methods, lucent foam blocks and ties, mouth gags and tongue forceps are required (Figure 5.6). At no time should the head be restrained manually with or without lead protection. To facilitate accurate positioning general anaesthesia is essential. It must be remembered that the endotracheal tube may obscure certain parts of the radiograph, especially in the VD/DV projections and so temporary extubation must be considered. At all times plain films must be taken before any contrast studies commence. Each of the projections that may be employed are mentioned with practical tips as to how to avoid common errors. Positioning details can be found in standard atlases of radiographic positioning (see Further Reading).

Plain lateromedial projection (LM)

Axial rotation of the skull and downward tilting of the mandible are the most likely faults. These can be

overcome by judicious use of lucent wedges under the mandible. The beam should be centred on the lateral canthus of the eye.

Plain ventrodorsal / dorsoventral projection (VD/DV)
There is no great advantage between these views, except in the brachycephalic breeds and cats where only the DV view is appropriate. Axial rotation of the animal is the most likely fault. Every effort should be made to align the animal from the tip of the nose to the tip of the tail in an accurately vertical position. The beam should be centred on the midline between the eyes.

Plain lateromedial oblique projection (LMO)
Oblique projections of the skull are of limited value in neurological cases. However, they will overcome superimposition of bilateral symmetrical structures, and are of especial use in the evaluation of temporomandibular joints, tympanic bullae and teeth. Most often they will be employed in the evaluation of the bullae. The animal is placed in lateral recumbency with the area of interest closest to the film. The skull is rotated through 20° along its long axis so that its dorsal midline approaches the table. The beam is centred on the base of the skull. A comparison view of the contralateral bulla is essential. Bullae should also be evaluated on the VD projections and/or the VD (open mouth) projection.

Plain ventrodorsal open mouth projection (VD open mouth)
The animal is placed in dorsal recumbency with no axial rotation. The mouth is drawn open by the tongue, which is pulled between the lower canines towards the sternum, by a pair of tongue forceps and a tie. Retraction of the tongue prevents a soft tissue opacity being cast over the bullae. The maxilla is retracted by a second tie ensuring that it creates an angle of 90° with the film. The beam is centred along the hard palate. Minor alterations in the angle of the beam from the vertical will overcome anatomical variations in the brachycephalic breeds. The animal must be extubated (Figure 5.7) otherwise the endotracheal tube might cast a shadow in the caudal nasal area that could be mistaken for a mass.

Plain skyline projection (SKYLINE)
Skyline (lesion orientated) projections of any lesion that disfigures the outer contour of the skull are essential to evaluate the involvement of deeper structures. Lucent positioning blocks are necessary for these views. The lesion is aligned at right angles to the beam and the beam centred on the midpoint of that lesion.

Plain foramen magnum projection
The animal is placed in dorsal recumbency with no axial rotation. The jaws are kept closed and the neck is flexed so that the hard palate creates an angle of 25°-40° to the vertical. The angle is dependent upon the breed/type. The beam is centred at the midpoint between the eyes, and exits through the foramen magnum. It is not necessary to extubate the animal, but severe kinking of the endotracheal tube can be overcome by employing special tubes with reinforced walls, which resist kinking.

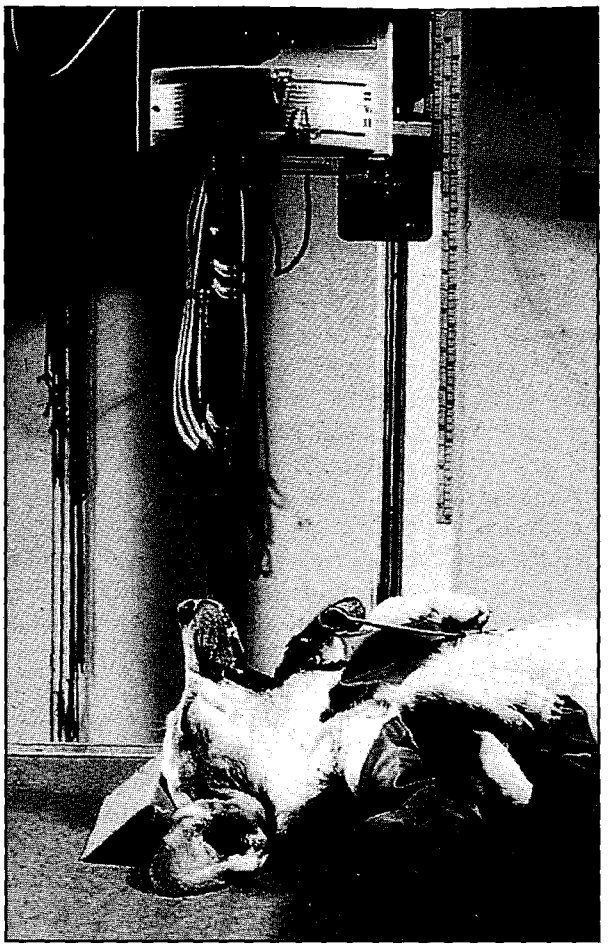


Figure 5.7: Positioning for VD (open mouth) view

Angular venography
The animal is placed in sternal recumbency and positioned as for DV views of the calvarium. Both angularis oculi veins are catheterised. This is not feasible in the brachycephalic breeds. The catheters are sutured or taped in place and three-way taps attached. Both jugular veins need to be occluded at the time of injection. This is best achieved by applying a rolled bandage to the jugular grooves on each side of the neck. An elasticated bandage around the neck will compress the rolls onto the jugular veins at the appropriate moment. Extension tubes should be attached to each three-way tap to prevent unnecessary X-ray exposure of the operator. Prior to the contrast injection, a plain film should be taken for comparison.

It is essential that the skull remains in exactly the same position during the contrast study, especially if subtraction techniques are to be employed. Whilst the jugular veins are occluded 3-6 ml of a WSCM (150-300 mg I per ml) are administered simultaneously via both catheters. The film is exposed immediately at the end of the injections. The contrast film can be studied in comparison with the plain film but, ideally, subtraction will allow the preparation of a radiograph on which only the contrast-filled cavernous venous structures at the base of the brain can be seen. Asymmetry of the vessels suggests the presence of a space occupying lesion. Subtraction techniques require special film and copying facilities and are only likely to be carried out in specialist centres. The availability of tomographic modalities (CT, MRI) render this rather crude technique obsolete.

Pneumoventriculography

Techniques involving the direct injection of air into the cranial ventricles have been described but are rarely employed. Recent non-ionic water soluble contrast agents such as iohexol are frequently seen to enter the subarachnoid spaces of the cranium during myelography with no ill-effects to the patient. Deliberate injection of these compounds into the ventricles has not been advocated. This technique has also been superseded by tomographic modalities (CT, MRI).

Radiographic Anatomy

Skull

The anatomy of the skull is complex and is further complicated by the wide variation of skull types encountered. These are usually divided into dolichocephalic ("long nosed"), mesaticephalic, and brachycephalic ("short nosed") types. Extremes of miniaturisation also influence skull conformation. Interpretation of skull radiographs is certainly facilitated by frequent reference to anatomical texts, radiographic atlases and, best of all, anatomical specimens.

Foramen magnum

In cases of occipital dysplasia, abnormal dorsal extension of the foramen magnum is seen, and is a common variant in toy and miniature breeds and may be of little clinical significance. Transverse tomographic slices (CT, MRI) are obviously ideal for this investigation.

Tomographic (CT/MRI) Anatomy

It is most convenient to image the skull from the cribriform plate to the foramen magnum employing transverse slices with the neck extended. This plane, in the human patient, would be termed frontal or coronal (face to back of head); the routinely collected transverse slices would image the top of the head to the base of the skull.

Radiology

Alterations in:-

Position

As nearly all radiographs will be taken of anaesthetised animals, changes of position will not be evident.

Size

Reduction in size (microcephaly, anencephaly) may occur as fatal congenital anomalies, but are unlikely to be the focus of radiographic attention. Symmetrical enlargements of the calvarium will occur in cases of hydrocephalus (Figure 5.8).

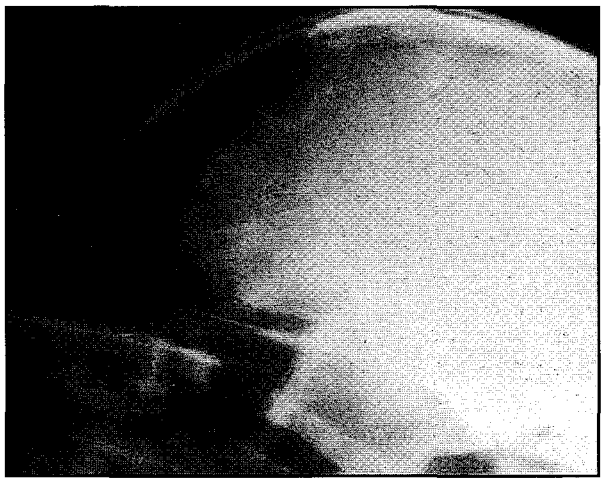


Figure 5.8: Hydrocephalus in this dog shows an enlarged, domed calvarium. Normal skull symmetry has been retained. The skull appears to have an almost homogeneous appearance, the normal convolutional markings that resemble beaten copper having been lost.

Number

Teratogenic anomalies are unlikely to be the focus of radiographic attention.

Contour

Congenital loss of the integrity of the calvarium does occur. Persistent fontanelles are not uncommon, especially in the Chihuahua, but are unlikely to alter the external contour of the skull. A craniofacial anomaly of the Burmese cat may result in protrusion of the brain through the defect (exencephaly), but this is unlikely to present as a radiological case. Mucopolysaccharidosis has been described in Siamese cats and can result in an alteration in facial and skull shape. Alterations in the shape of the foramen magnum have already been discussed. Acquired alterations in contour are most likely to be of traumatic or neoplastic origin (Figure 5.9), and may assume an infinite number of appearances. When this alteration in contour involves the calvarium it may impinge upon neural tissue. Fractures of the canine skull are less frequent than in man because of the relatively thicker bone. When looking for fractures, a careful assessment of the soft tissues for focal areas of swelling may well draw the eye to the

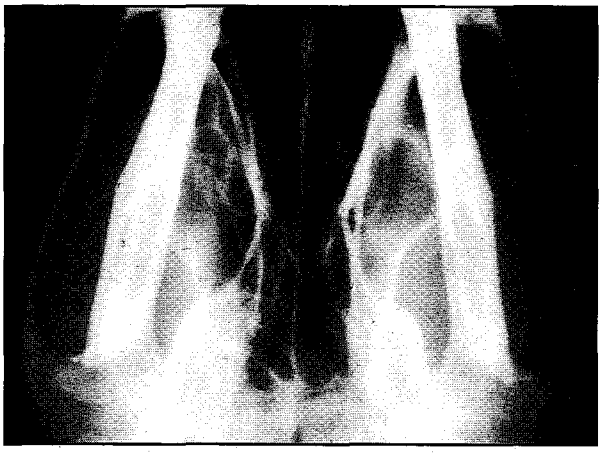


Figure 5.9: The contour of the right zygoma has been lost because of a fracture in this dog following a fight. A focal lucency is evident at the fracture site.

bony lesion. Similarly protrusions of the eyeball may well signal retrobulbar lesions.

Architecture

Both the internal and marginal architecture of the skull are probably impossible to assess and so changes in opacity and contour, only, can be evaluated.

Diffuse decrease in opacity

Generalised decrease in bony opacity is most likely to occur in cases of hyperparathyroidism (Figure 5.10). This may be primary as a result of hyperplasia or neoplasia of the parathyroid glands or, more commonly, secondary as a result of dietary mismanagement or chronic renal disease. Changes in the skull are particularly prevalent in renal secondary hyperparathyroidism. The hydrocephalic skull will be enlarged ("stretched") and will appear to have a decreased opacity with loss of the convolutional markings of the calvarium (Figure 5.8).

Focal decrease in opacity

Focal decreases in opacity may be encountered in congenital anomalies, fractures, osteomyelitis and neoplasia.

Multiple decrease in opacity

Multiple lucencies are characteristic of multiple myeloma, but are likely to be obvious in thinner areas of the skeleton before the skull. Other neoplasms, particularly soft tissue tumours invading bone, and osteomyelitis may result in multiple lucencies.

Diffuse increase in opacity

Osteopetrosis, a rare hereditary condition affecting the axial and appendicular skeleton, has been reported but probably the most common cause of a diffuse increase in opacity is craniomandibular osteopathy (Figure 5.11). This disease, seen in young West Highland white terriers, other small terriers and a few other breeds, is unlikely to accompany neurological signs.

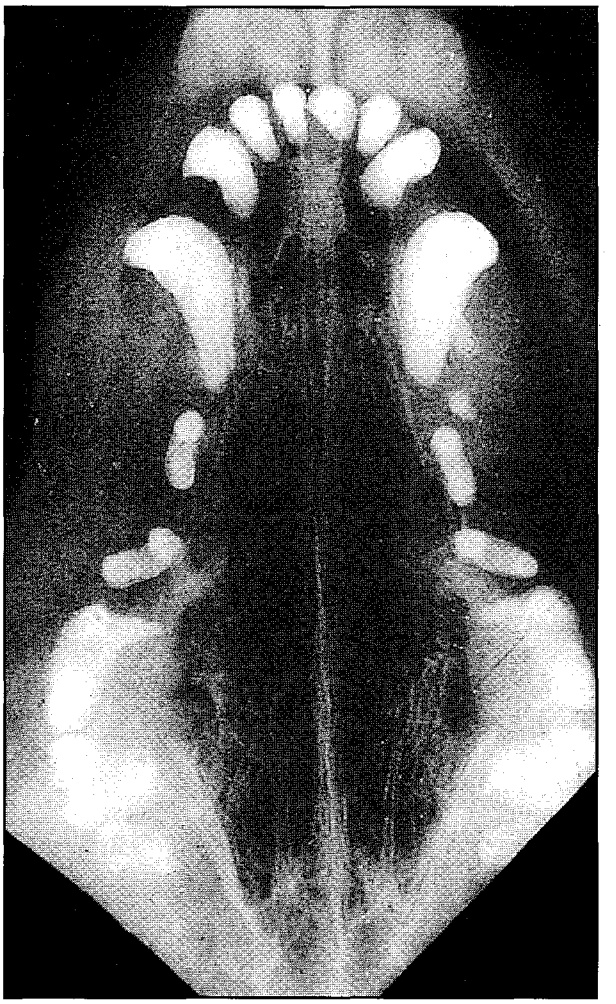


Figure 5.10: There is a generalised decrease in mineral density in the skeleton. Spinous processes and vertebral bodies would be especially lucent, and "pathological" fractures might occur in the ribs and the lumbar spinous processes. These changes are typical of hyperparathyroidism. Changes affecting the skull are more often seen in those cases associated with renal disease ("Rubber jaw"). Because of the loss of mineralisation within the skull, the fine turbinate pattern appears exaggerated and the teeth appear to be "floating in mid air" as the alveolar bone is almost invisible. This is typical of a case of renal secondary hyperparathyroidism.

Metaphyseal osteopathy, a metabolic bone disease of the long bones of large growing dogs, can affect the skull causing diffuse increase in opacity.

Focal increase in opacity

Osteosarcoma, osteoma and osteochondroma, may all lead to focal areas of increased opacity. More advanced cases of otitis media will lead to a bony reaction to the chronic infection within the middle ear. The walls of the affected bulla and the adjacent petrous temporal bone may become sclerotic. Additionally, the air contrast within the bulla may be lost, being replaced by a soft tissue opacity indicating the presence of exudate or granulation tissue. (Figure 5.12). An area of increased opacity of the calvarium is sometimes seen over meningioma lesions in cats.

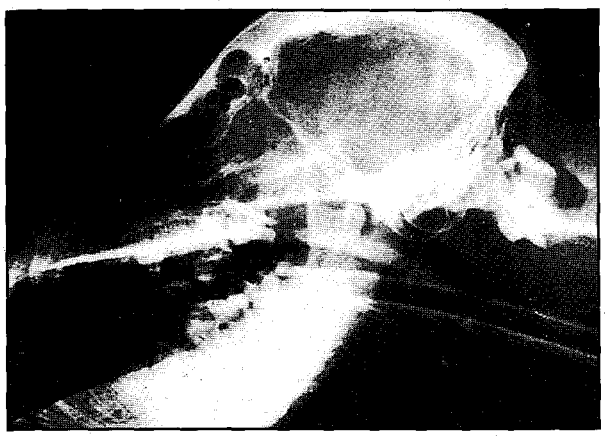


Figure 5.11a: *In this lateral view of the skull of a West Highland white terrier with craniomandibular osteopathy, there is a diffuse thickening of the dome of the calvarium and the mandibles, but in this case little change in the tympanic bullae.*

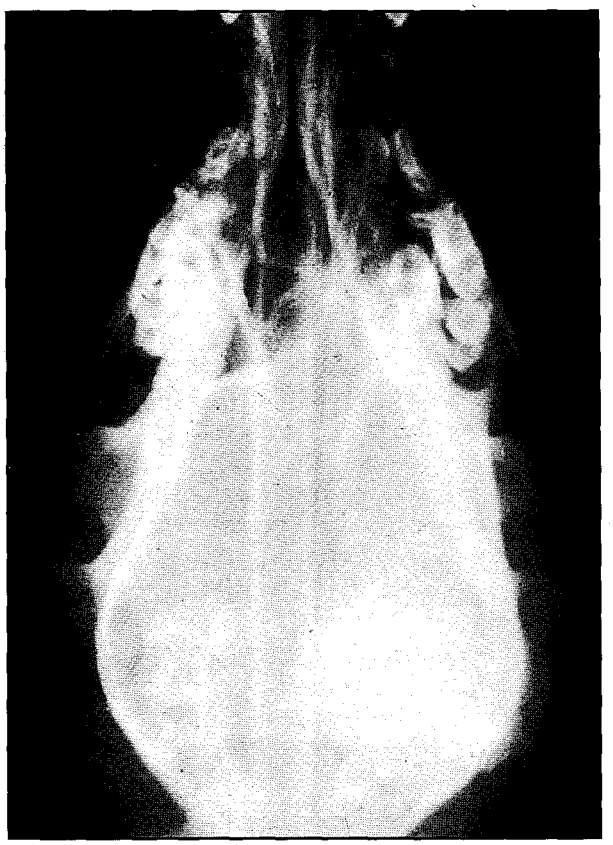


Figure 5.11b: *In this VD view of a different dog, new bone deposited on the left bulla particularly is typical of craniomandibular osteopathy.*

Multiple increase in opacity

Osteoblastic metastases may result in multiple areas of increased opacity.

Mixed changes

Mixed osteodestructive and osteoproductive changes may often be encountered. Neoplastic processes that affect the skull can be outrageously bizarre on some occasions contain areas of both increased and decreased opacity (Figure 5.13).

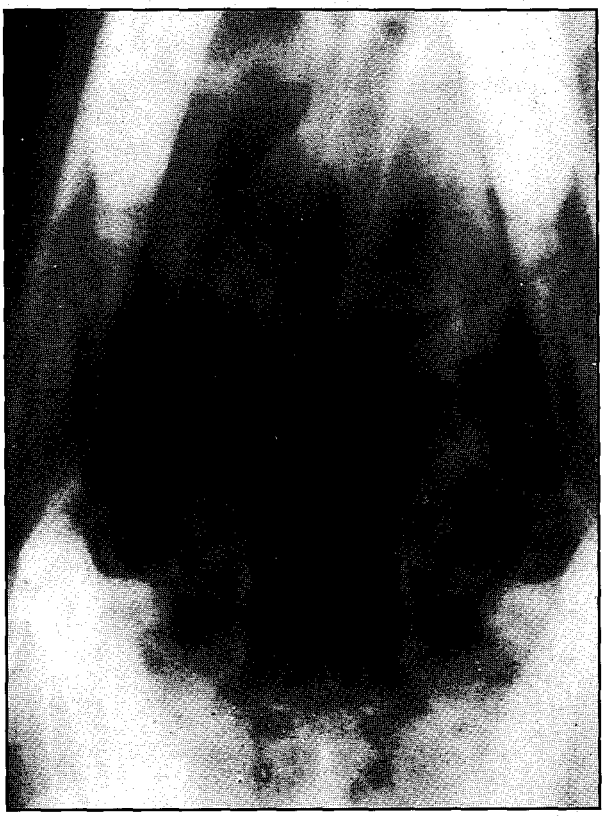


Figure 5.12: *VD (open mouth) view of the tympanic bullae show the left bulla to have an increase in soft tissue density within it, due to the presence of granulation tissue and/or exudate. A slight increase in thickness of the bony wall is also noted.*

Figure 5.13: *Bizarre expansile lesion destroying the skull dorsally and showing mixed proliferative and destructive elements. This is a malignant bone tumour of the skull (osteosarcoma)*

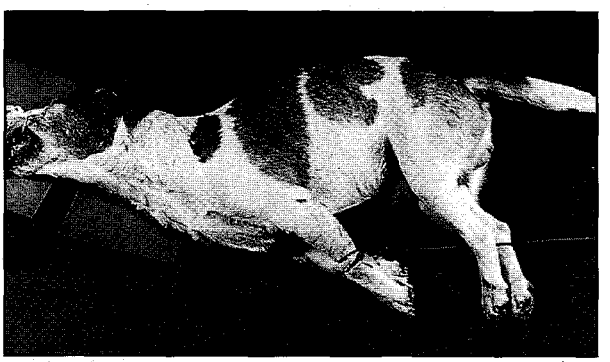
SPINE

Techniques

Only bony structures are visible, and to minimise the difficulty arising from the complex anatomy, accurately positioned lateral and ventrodorsal films are essential. Myelography and other contrast techniques

such as epidurography, intraosseous venography and discography help in the evaluation of the spinal cord and spinal nerves. The reader is referred to atlases of positioning, but practical tips for each of the projections are given.

Plain lateromedial cervical projection (LM)
The animal is placed in lateral recumbency with the thoracic limbs tied back tight against the sternum. The neck is partially extended. Axial rotation must be avoided, usually by wedging the sternum and the skull. Dipping of the cervical spine over the film is best avoided by placing a small lucent wedge under the mid part of the neck (Figure 5.14 and 5.15). The



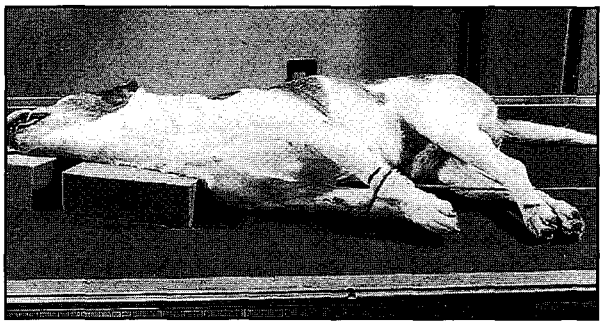


Figure 5.14 and 5.15: Positioning for lateral views of the cervical spine. Foam wedges ensure that the whole of the cervical spine is horizontal to the table. There should be no axial rotation. The thoracic limbs are drawn caudally and the neck extended, to prevent superimposition of the scapulae and associated soft tissues on the caudal cervical vertebrae.

beam is centred on the area of interest. It is necessary to take at least two lateral views (C_1-C_4 and C_4-C_7) to overcome geometric distortion and the different exposure factors needed for the cranial and caudal portions of the neck. Coned views of the area of interest may also be made. This is the best projection for evaluation of the intervertebral disc spaces.

Plain lateromedial flexed cervical projection (LM-FLEX)
Lateral views of the neck in the force flexed position may exaggerate malalignment of adjacent vertebrae. Extreme care should be taken if atlantoaxial instability is suspected or fracture dislocations are present, as further soft tissue damage may be caused during radiography.

Plain lateromedial extended cervical projection (LM-EXT)
This projection may also exaggerate malalignment and the caveats mentioned above stand.

Plain lateromedial distracted/relaxed cervical projection (LM-DISTRACT/RELAX)
In cases of caudal cervical spondylomyelopathy it can be useful to assess the possible effects of distraction on a bulging disc anulus / longitudinal ligament. It is convenient on a tilting table to suspend the animal first by the head alone (distracted) and then by the thoracic limbs with the head loose (relaxed). Should the protrusion into the vertebral canal diminish with distraction it implies that a surgical distraction technique will be beneficial. The techniques are only of value during myelography.

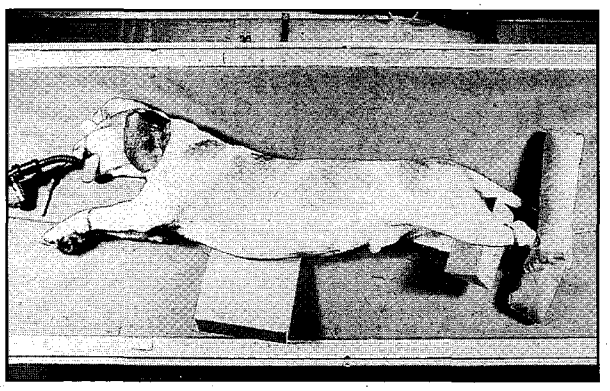
Plain ventrodorsal cervical projection (VD)
The animal is placed in dorsal recumbency with no axial rotation and the neck extended over the film. Appropriate angulation of the beam will allow accurate penetration of the disc spaces, but this is often an unhelpful view in cases of disc disease.

Plain dens projection
The positioning described for the plain ventrodorsal open mouth projection (see above) is used but it may be necessary to angle the beam at about 10° in a DV direction to the hard palate.

Plain lateromedial thoracic projection (LM)
The animal is placed in lateral recumbency with the limbs forcibly tied cranially and caudally. Axial rotation must be prevented, any natural dips in the spine must be padded and the limbs are best separated by foam pads so that they remain parallel to each other and parallel to the table (Figure 5.16 and 5.17). Several views will be necessary to evaluate the whole of the thoracic spine.

Plain ventrodorsal thoracic projection (VD)
Ventrodorsal films of the thoracic spine are difficult to interpret, because of the superimposition of the sternum and mediastinal structures. However, they should not be ignored routinely. The thoracic and pelvic limbs are tied cranially and caudally, so that they are parallel to each other, and axial rotation of the whole spine prevented with the judicious use of lucent foam wedges and pads.

Plain lateromedial thoracolumbar and lumbar projection (LM)
Positioning is as for the lateral thoracic spine with appropriate centring.



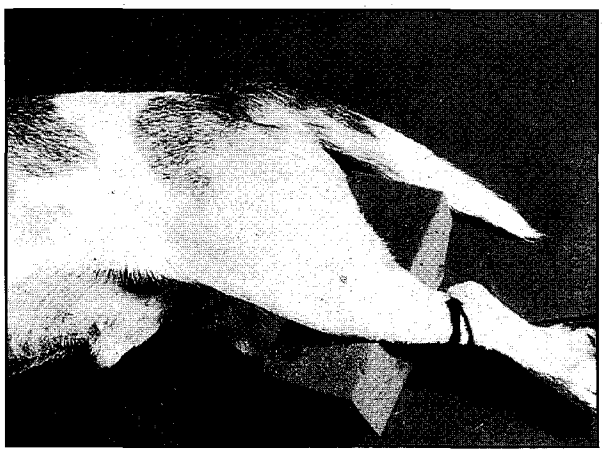


Figure 5.16 and 5.17: *Positioning for lateral views of the thoracic, thoracolumbar and lumbar spine. The spine is forcibly extended with ties. Axial rotation is corrected by padding the sternum. Foam pads between the pelvic limbs help overcome rotational distortion.*

Plain ventrodorsal thoracolumbar and lumbar projection (VD)

Positioning is as for the ventrodorsal thoracic spine (see above) with appropriate centring. The absence of radiodense overlying structures makes these useful films.

Plain lateromedial lumbosacral projection (LM)

Positioning as for the lateral thoracic spine (see above) with the beam severely collimated and centred on the lumbosacral joint.

Stressed lateromedial lumbosacral projection (LM-STRESSED)

The spine can be maximally flexed by tying the thoracic limbs caudally and the pelvic limbs cranially so that the dog adopts a position similar to a racing greyhound in full flight. Maximum extension can be achieved by tying the thoracic limbs dorsocranially and the pelvic limbs dorsocaudally, arching the lumbosacral articulation against a fixed, rigid object e.g. sandbag on the X-ray table. The latter view has been thought to mimic the manoeuvre that most pains dogs with lumbosacral spondylopathy and might therefore be a significant stressed view (see "Changes in position" below).

Myelography

Myelography is a safe procedure providing the operator is able to penetrate atraumatically the subarachnoid space. The new non-ionic water soluble contrast media (metrizamide, iopamidol, iohexol, iotrolan) are all extremely safe. Iohexol is the safest and the cheapest.

Short bevel spinal needles are best for making the injection, although ordinary hypodermic needles will suffice. Contrast containing 300-350 mg Iodine per ml is used in doses varying from 1 ml -10 ml, depending on the size of the animal and the expected location of the lesion. Puncture of the subarachnoid space can be made in the mid to low lumbar area or via the cerebellomedullary cistern (cisterna magna). The cisternal route is often preferred, as it is technically simpler and probably carries a lower morbidity and chance of technical failure. Only if the limits of a totally obstructive lesion need to be determined is it necessary to make a lumbar puncture. In those animals with lesions that are predicted to be large and space occupying that will almost certainly obstruct the flow of contrast from a cisternal puncture, lumbar puncture may be the first choice. Such cases would typically include thoracolumbar disc herniations causing severe neurological disability. As with all contrast examinations, it is essential to precede myelography with a satisfactory set of plain films.

Cisternal myelography

Cisternal puncture is described in Chapter 4. During cisternal puncture it is necessary to flex the neck forcibly, thus kinking the endotracheal tube. It is possible to employ tubes with specially reinforced walls, which resist kinking. Alternatively, releasing the inflatable cuff during neck flexion allows the animal to breathe around the tube.

Lumbar myelography

Most descriptions of lumbar puncture suggest that the patient is positioned in accurate lateral recumbency with the lumbar spine maximally flexed. This can make anatomical landmark recognition, particularly the midline, difficult especially in fat or very large breeds. Alternatively the patient can be sat on its perineum with the pelvic limbs drawn forward and the spine flexed. Recognition of midline structures is much easier in this position.

The landmarks of note are the midline dorsal spinous processes and the wings of the ilia. The injection is usually made at L_5/L_6 in dogs (L_6/L_7 in cats). The spinous process of the sacrum is short and below the level of the iliac wings. The spinous process of L_7 is short but usually just palpable and the spinous processes of L_6 more readily palpable. It is likely therefore that the injection site will be between the two most caudal easily palpable spinous processes. A long, short bevel spinal needle is required (e.g. 20G x 3.5"). The needle is advanced

through the aseptically-prepared skin site just lateral to the spinous process of L_6. The process can be used as a guide to prevent the needle track straying from the midline, by sliding the needle down beside it. The needle angle is usually about at right angles to the skin but directed a little cranially with reference to the spine. The portal of entry will be the interarcuate space between L_5 and L_6. If bone is hit, the needle can be withdrawn slightly and redirected. With practice a slight "popping" sensation will be felt when the needle traverses the ligament and the dura mater. This is not as obvious as it is in the cerebellomedullary cistern, but the experienced operator will come to recognise it. Further advancement of the needle will cause it to traverse the neural structures (spinal cord or cauda equina depending on level), usually making the pelvic limbs twitch. This is should not cause the operator or assistant horror, but be viewed as an indication of accurate placement of the needle! The needle can then be advanced until it strikes bone of the ventral vertebral canal. At this point the stilette can be withdrawn, and if the needle is backed off slightly a small volume of CSF should be apparent, confirming patency with the thecal sac. If the first penetration of the thecal sac is sensed, then CSF will flow and contrast can be injected dorsal to the neural structures. If not, a ventral injection is usually made. The possibility of a central canal injection increases if the injection is made cranial to L_5/L_6 (see below). The volume injected will depend upon the expected location of the lesion and the size of the patient, but is generally about 50-75% of that used for cisternal injections. With large obstructive lesions the contrast can be forced past by this technique, overcoming the problems of severe cord swelling. However if resistance is felt during injection or if the animal becomes distressed (e.g. increased respiratory rate) while the injection is being made it is best to terminate the injection at that point.

Various technical problems can occur during myelography and bear discussion, as the technique is being used more widely by the general practitioner.

1. Problems associated with needle puncture of the subarachnoid space

Accurate needle placement needs practice, and repeated needle puncture in the same patient can lead to problems. These may involve haemorrhage and difficulty in establishing whether a clean connection with the CSF has been made. Over-penetration at the cisternal site may cause the spinal cord to be damaged. A single needle track is thought to be relatively harmless, but repeated injuries that are more likely to occur in the technique that is not "going smoothly" could be damaging. The needle could damage vital structures if they are prolapsing through the foramen magnum, and if such a condition were suspected in advance, cisternal puncture should be avoided. It is possible to penetrate the cord and connect with the central canal. Here CSF may flow, suggesting to the operator that needle placement is correct. In cases where a malformation involving hydromyelia is present this flow may be substantial. Injection of "normal myelographic" volumes of contrast into the central canal could be fatal or cause serious arachnoiditis. The incidence of central canal injection is higher with lumbar punctures, especially if performed cranial to L_5/L_6.

2. Problems associated with contrast media

The choice of the correct contrast medium and concentration is vital. Ionic media will almost certainly result in fatalities. The appearance of non-ionic media such as Ultravist® just further confuse the issue, as this is contraindicated for myelographic use.

Poor mixing of the contrast with the CSF can cause patchy filling. This can be minimised by warming the contrast to body temperature before injection. The speed of injection may also make a difference. Historically, slow injections over several minutes have been advocated, but there is a subjective impression that rapid administration may result in a better "bolus" effect. Some workers repeatedly draw back and re-inject in an attempt to improve mixing. A recent myelographic agent iotrolan (Isovist®) has been suggested to give a better "bolus" effect. Mixing can sometimes be improved by rotating the patient and making exposures at 180^0 to the original can sometimes improve mixing and filling. The rate of flow of the contrast agent in the subarachnoid space will be a function of physiological, pathological and gravitational effects, and only experience and a knowledge of the expected lesion can negotiate these variables. A frequent site of poor filling with cisternal injections is the cervicothoracic junction, and putative filling defects at this level should be considered with suitable caution. If in doubt a further injection on the same day or on another occasion can be made. Injection at the "other" site can also be helpful in equivocal cases.

3. Seizures

Seizures were commonplace when metrizamide was used, and the protocol that incorporated diazepam as the premedicant of choice was adopted. The incidence of seizures has been much reduced with iopamidol and iotrolan, and with iohexol particularly. Routine premedication is acceptable with these media and raising the animal's head during recovery will help minimise seizures. If recovery is accompanied by hyperaesthesia, one IV dose of diazepam is usually sufficient to allow a gentle recovery. The removal of a volume of CSF equivalent to the dose of contrast to be administered has been advocated but is not an essential precaution.

Vertebral sinography (Lumbar sinus venography, intraosseous vertebral venography)

Techniques involving the filling of the lumbar internal vertebral venous plexus (venous sinuses) to evaluate vertebral canal structures in the lumbosacral area have been described. Most commonly, an injection of contrast is made via a bone marrow needle inserted into one of the caudal vertebrae. If the caudal vena cava is compressed during the injection, the venous plexus will fill better with contrast. It is seldom necessary to consider this techniques.

Epidurography

During subarachnoid injection of contrast media an epidural injection may inadvertently occur. The images thus derived are often confusing. Deliberate epidural injection has been described. This technique has limited applications, but can provide information in cases of lumbosacral disease especially when the thecal sac terminates cranial to the lumbosacral joint, or when information about the lumbar nerve roots is required (Figure 5.18).

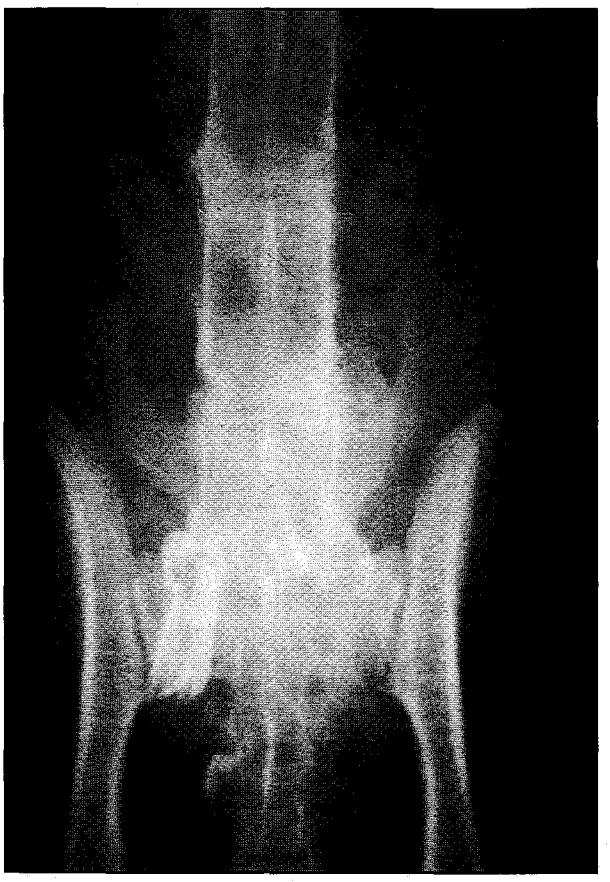


Figure 5.18a: *Dorsoventral epidurogram of a cat. The nerve roots on the left of the fiure have been outlined and have failed to be outlined on the right of the figure.*

Like lumbar puncture, this technique can be made with the dog in lateral recumbency. Alternatively the dog can be in sternal recumbency. The injection can be made through the interarcuate ligament at the lumbosacral joint or first four intercaudal joints. The shortness of the L_7 and sacral spinous processes and the iliac wings are again used as landmarks. The cranial-most caudal vertebrae may be palpable. The needle is advanced into the vertebral canal and the stilette removed. Test injection of air or saline, or contrast should meet with no resistance. Resistance implies incorrect placement. A test radiograph can be taken to assess success. As lesions at this level are often lateralised, the DV/VD view may be most helpful. It may therefore be the best routine to perform the needle placement, injection and test radiograph with the dog in sternal recumbency (DV projection). If the contrast injection has been successful, the lateral, stressed lateral and VD views can then be undertaken.

Figure 5.18b: *The post mortem slide shows the grossly thickened right nerve root arising from the cauda equina (right of the figure).*

Discography

Direct injection of positive contrast media into discs, especially the lumbosacral disc, has been described, but it is a technique with limited applications.

Radiographic Anatomy

Atlas (C_1)

The atlas is a short vertebra with prominent lateral

processes. In ventrodorsal projection the lateral foramina, through which the spinal arteries pass, are present in the lateral processes.

Axis (C_2)
The axis is the largest cervical vertebra. It is an elongate bone with a thin, relatively lucent spinous process. Projecting from the cranial margin of the axis in the midline is the dens (odontoid peg). This is sometimes visible on lateral views, but more often has to be inspected on the VD or special views. There is no intervertebral disc between C_1 and C_2.

Cervical vertebrae
The remainder of the cervical vertebrae are all similar. The spinous processes increase in size caudally. The lateral processes project cranially, often intersecting with the preceding intervertebral disc space. These are often confused as mineralised disc material or bony fractures. The lateral processes of C_6 are especially large and project ventrally. The C_2-C_3 disc space is the largest, the others are of similar size to each other, although C_7-T_1 normally is smaller. Linear lucencies occasionally are seen in the cervical vertebrae and are thought to be the passage of nutrient vessels. In VD projection, the shadow cast by the laryngeal cartilages may give a false impression of the presence of a radiodense foreign body. The ventral column of a myelogram normally "kinks" and narrows over the C_2-C_3 intervertebral disc space. Linear lucencies seen in the myelographic shadow represent the origin of spinal nerve roots. There is a natural expansion of the spinal cord at the level of the brachial plexus (C_6-C_7). The cranioventral borders of the bodies of vertebrae C_5-C_7 are frequently deformed in those breeds that are prone to cervical spondylopathy. The cranioventral margin has a "step like" appearance leading to poor support of the disc anulus fibrosus. Not surprisingly, the associated discs often rupture later in life.

Thoracic vertebrae (T_1-T_{13})
The thoracic vertebrae are all similar, possessing specialised facets for the articulation of the rib heads. The spinous processes are prominent and project caudally from T_1-T_{10}, the spinous process of T_{11} (the anticlinal vertebra) projects dorsally, and those of the remainder project cranially. It must be remembered that between the heads of ribs 2-10, a radiolucent intercapital ligament exists. This reinforces the longitudinal ligament making dorsal disc herniation unlikely.

Lumbar vertebrae (L_1-L_7)
The lumbar vertebrae are all similar and relatively simple to evaluate. Myelographically, there is a natural enlargement of the spinal cord at the site of the lumbosacral outflow (L_4-L_5 vertebrae). From this point on, the diameter tapers and elongate lucencies represent the "tails" of the cauda equina. Anatomical variants such as transitional vertebrae (lumbarised sacral segments or "extra" lumbar vertebrae) may predispose to degenerative disease at this level.

Sacrum
The sacrum comprises three fused vertebrae that articulate with the ilia. Its shape and position is variable. A normal myelographic column will penetrate the sacral canal in most (> 85%) patients.

Caudal vertebrae
These are variable in size, shape and number in different breeds.

Radiology
Changes in:-

Position
The position of various segments of the vertebral column may be altered in congenital and acquired luxations and fractures (Figure 5.19). The relative positions of L_7 and the sacrum can alter with transitional vertebral anomalies. The position of the lumbosacral thecal sac varies in some individuals, terminating within L_7. The author has found that forcibly extended lateral views of the lumbosacral joint can cause thecal contrast to be extruded from the area of interest, even in normal dogs, and so this myelographic finding must be interpreted with great care in suspected cases of lumbosacral spondylopathy.

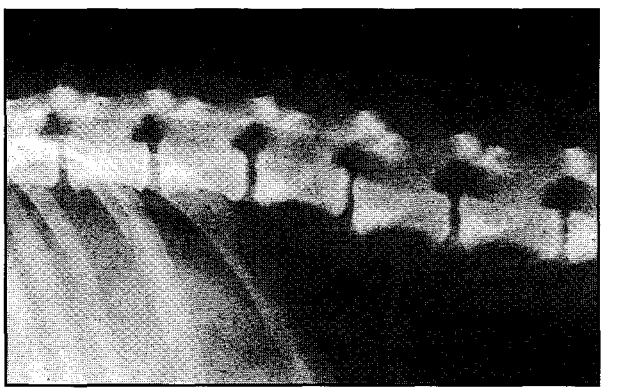


Figure 5.19: *An intervertebral luxation at L_2-L_3 has resulted in a step deformity in the alignment of these vertebral segments. Also noticeable are a narrowing of the disc space, a reduction in size of the intervertebral foramen, and an increase in the width of the associated apophyseal joint.*

Size
Vertebrae may collapse in osteodestructive disease such as metabolic osteopaenias and neoplasia. Trauma and infection may also lead to an apparent reduction in size (Figure 5.20).

Number
The archetypal number of vertebrae in the dog and cat are:- cervical: 7, thoracic: 13, lumbar: 7, sacral: 3 and caudal: 6-20. There may be an apparent change in number, as congenital transitional vertebrae occur. At

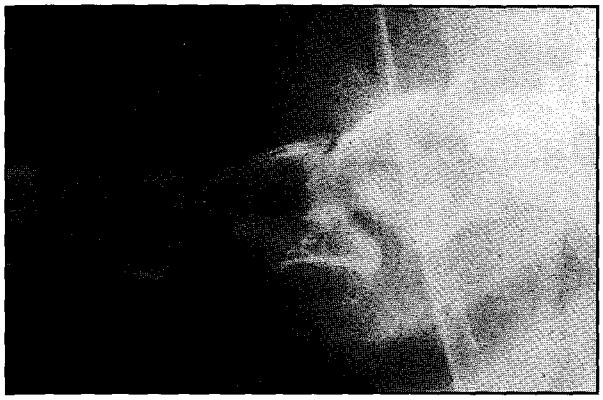


Figure 5.20: *At C_7 the vertebral body length has reduced giving the vertebra a more square shape. The internal architecture of the body has also been disrupted. Collapse of this vertebra is occurring because of an osteodestructive neoplasm (osteosarcoma).*

the junction of one section of spine to another, a vertebra may assume characteristics of both sections, e.g. a first lumbar vertebra with vestigial ribs, a lumbarised sacral vertebra with transverse processes (Figure 5.21). At first glance it will appear as if there is an abnormal number of vertebrae. This is unlikely to have any clinical significance, but may cause some alteration in the overall alignment of the spine. Lumbosacral transitional vertebrae will occasionally make it difficult to align the pelvis accurately for a VD view of the hips, and their presence may predispose to lumbosacral disease.

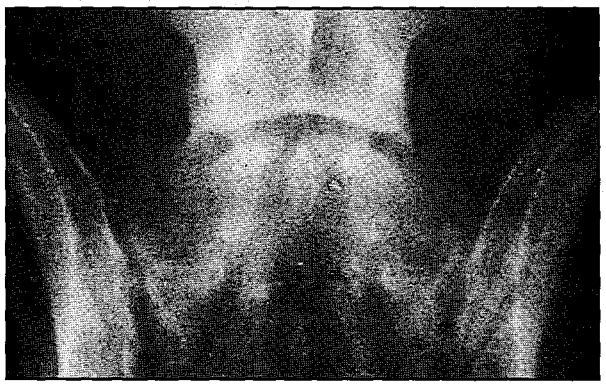


Figure 5.21: *In this dog a vertebral segment within the pelvis has short curved transverse processes. The dog had seven normal lumbar vertebrae, and so this is probably a lumbarised sacral segment - a transitional vertebra. These are sometimes associated with lumbosacral spondylopathy, but further evidence is required to make this diagnosis. Also, asymmetric lumbosacral transitional anomalies will often be associated with some pelvic asymmetery, rendering accurate positioning for VD hip films difficult, if not impossible.*

Contour - Spine

Curvature of the spine may occur in any one of three directions or sometimes a combination of these. Scoliosis is a lateral curvature in the horizontal plane when viewed from above (Figure 5.22). Kyphosis is a dorsal curvature in the vertical plane when viewed from the side (Figure 5.23). Lordosis is a ventral curvature in the vertical plane when viewed from the side (Figure 5.24). These deviations may be so severe that the neonate is not viable but, more often than not, they are subclinical. As the animal gets older and heavier, they may be accompanied by degenerative changes that lead to clinical signs.

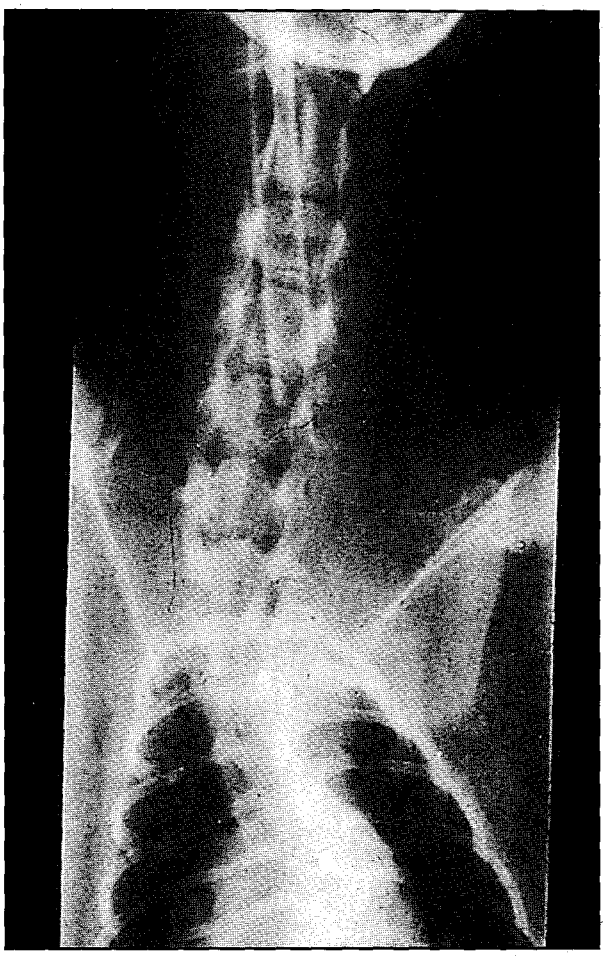


Figure 5.22: *Curvatures in the horizontal plane, here at the thoracic inlet and over the base of the heart, are called scoliosis.*

Figure 5.23: *A gross deformity of L_4 and to a lesser extent the adjacent vertebrae, has led to a kinking of the spine (convex dorsally). This deformity has resulted from a hemivertebra and is called kyphosis.*

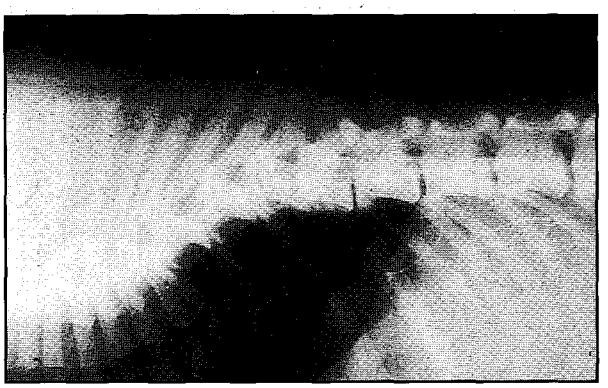


Figure 5.24: Vertebral anomalies in mid and caudal thoracic vertebrae have led to an overall dipping of the spine (convex ventrally). This deformity is called lordosis.

Contour - Vertebrae

Individual vertebrae may have an altered shape, they may be transitional or block (two segments congenitally fused) but do not cause clinical signs (Figure 5.25). However, congenital malformations of the hemivertebra type ("wedge", "butterfly", spina bifida, congenital absence of the dens) may be associated with neurological deficits.

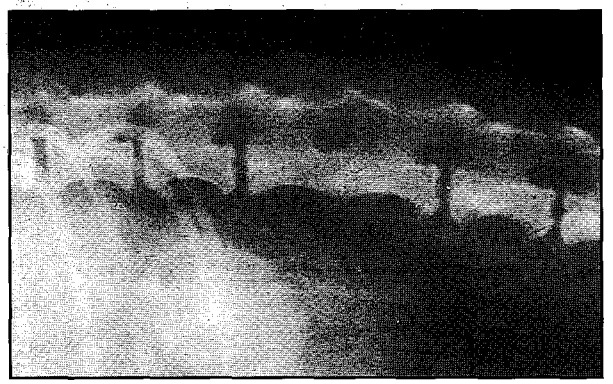


Figure 5.25: An incidental finding during a urinary investigation revealed a congenital fusion of L_2 and L_3. These malformations are usually of no clinical significance.

Acquired alterations in contour may arise from fractures, osteomyelitis or neoplasia.

Architecture

Both the internal and marginal architecture of the vertebrae are difficult to assess, so changes in opacity and contour are of greater significance. Osteodestructive changes associated with neoplasia and osteomyelitis are the most likely to alter the architecture (Figure 5.26).

Diffuse decrease in opacity

Generalised decrease in bony opacity may be associated with disuse osteoporosis, primary and secondary hyperparathyroidism, hyperadrenocorticalism, steroid overdosage, and mucopolysaccharidosis (Figure 5.27).

Focal decrease in opacity

Focal infective or neoplastic lesions may lead to a decrease in opacity. The lesion may be primarily within bone, or may extend into the vertebra from the surrounding soft tissues (Figure 5.28 and 5.29)

Figure 5.26: The marginal architecture in L_2 has been lost, in as much as the spinous process and dorsal arch have been destroyed. The internal architecture has also been affected, as the remnants of the lateral aspects of the neural arch are being eroded as a result of an osteodestructive lesion.

Figure 5.27: Generalised loss of mineral opacity occurs in hyperparathyroidism, in this case secondary to inappropriate diet. The radiograph, at first sight, appears poorly exposed or processed. This is because there is little contrast between soft tissues and the poorly mineralised skeleton.

Multiple decrease in opacity

Multiple lucencies are likely to arise from round cell series tumours e.g. multiple myeloma (Figure 5.30).

Diffuse increase in opacity

Osteopetrosis has already been mentioned (see above). A more common cause of diffuse increase in opacity is hypervitaminosis A in the cat, where massive, proliferative bony deposits may affect any part of the axial or appendicular skeleton, but especially the cervical spine (Figure 5.31). Similar radiographic changes have been seen in mucopolysaccharidosis in Siamese cats.

Focal increase in opacity

Focal increases in opacity arise from osteoblastic activity resulting from neoplasia or in response to infection. The primary lesion may be within the vertebra but the sclerosis could well be an attempt by the vertebra to keep out a neoplastic or infective process (Figure 5.32).

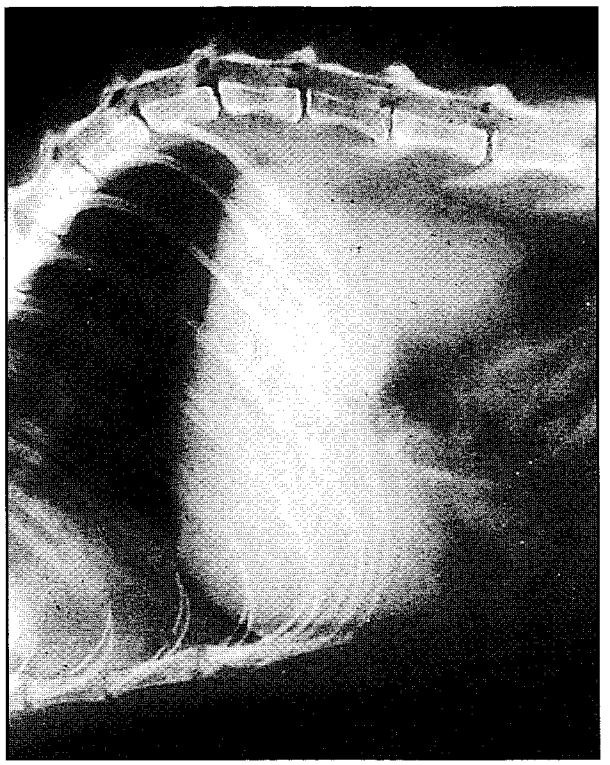


Figure 5.28: *There is some loss of opacity in the mid portion of the vertebral body of L_3. Some marginal proliferation of fluffy new bone has also occurred ventrally. These changes are associated with a focal osteomyelitis.*

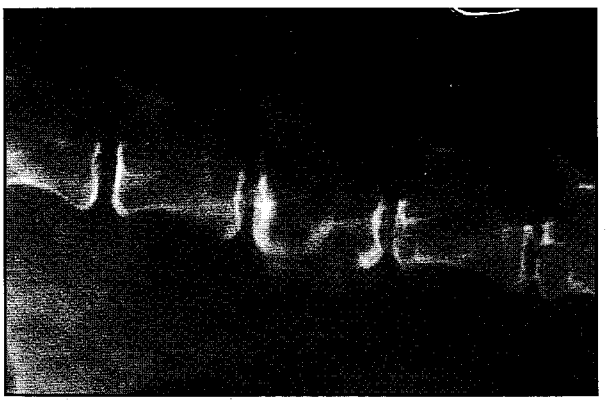


Figure 5.29: *Focal lucencies within the vertebral body and neural arch of L_4 in this West Highland White Terrier have been caused by myeloma. An amorphous mineralisation of soft tissues is evident ventral to the vertebral body.*

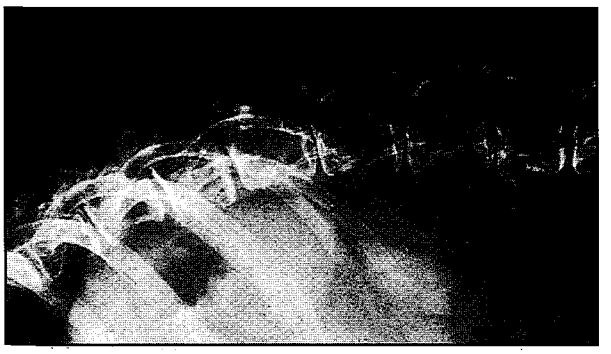


Figure 5.30: *Multiple punched out focal lucencies are seen throughout the spine in this dog as a result of multiple myeloma.*

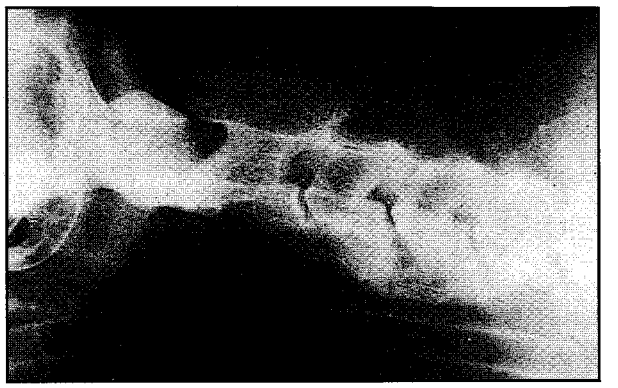


Figure 5.31: *Diffuse, well defined deposits of new bone are present along the ventral aspects of the cervical vertebrae in this cat. This has resulted from a diet rich in liver (hypervitaminosis A).*

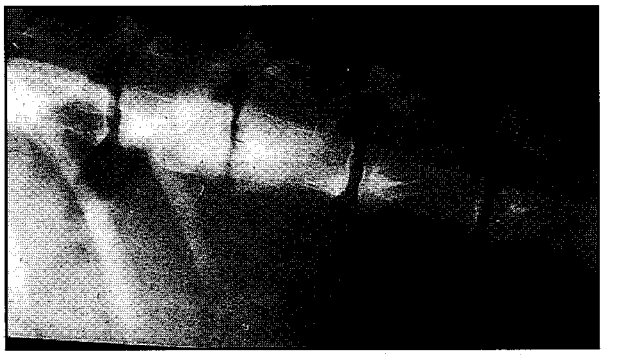


Figure 5.32: *In this dog the L_2-L_3 disc space has collapsed as a result of a septic focus (discospondylitis). In an attempt to wall off the infection, the vertebral end plates either side of the affected disc have become more dense (sclerotic).*

Multiple increase in opacity

Osteoblastic metastases may result in multiple areas of increased opacity.

Intervertebral Joints

There are essentially two types of joint in the vertebral column - the intervertebral joints and the apophyseal (synovial) joints. Similar criteria can be used to evaluate these joints, as have already been discussed in the introduction.

Decrease in size of the intervertebral disc space and/or the intervertebral foramen

If the disc deforms and herniates, the disc space and/or intervertebral foramen will narrow (Figure 5.33). Comparison of immediately adjacent segments of the spine is necessary. Often, in more subtle cases, it is easier to appreciate a change in shape of the intervertebral foramen than the disc space itself. Fractures and dislocations may lead to a decrease in size. It must be remembered that quite gross displacements of the spine in one plane may be almost invisible on the right angle view. Chronic infection centred on the disc (discospondylitis) will eventually lead to a reduction in the size of the disc space. However, the most common reasons for an apparent reduction in size is an oblique or inaccurately centred radiograph.

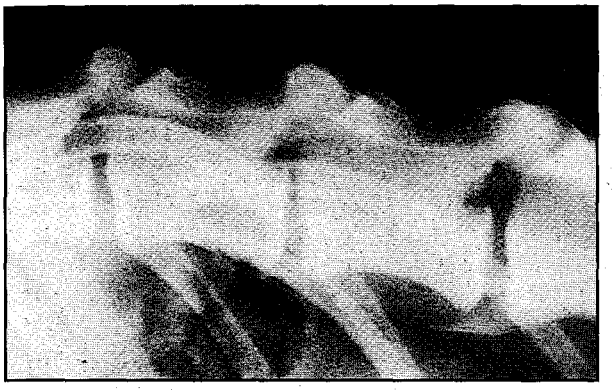


Figure 5.33: The T_{13}-L_1 disc space is narrower than the adjacent disc spaces. The associated neuroforamen has also reduced in size and has lost its characteristic "Scottie's head" shape. Mineralised discs are noted at T_{10}-T_{11} and T_{11}-T_{12}. These may well be clinically quiescent and only confirm the presence of degenerative disc disease. The narrowed disc space is much more likely to be clinically significant.

Increase in size of the intervertebral disc space and/or the intervertebral foramen

In the early stages of discospondylitis, lysis of the adjacent end plates of the two vertebrae will lead to an increase in the size of the disc space (Figure 5.34). Fractures, dislocations and some neoplasms can increase the size.

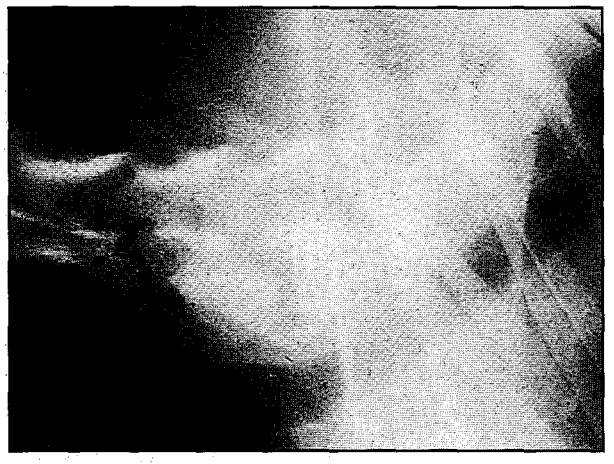


Figure 5.34: In this dog an aggressive and active septic focus in the C_6-C_7 intervertebral disc space has led to destruction of the adjacent vertebral end plates. This gives an impression of an increase in size of the disc space. Note that the margins are ragged, and ventrally and dorsally new bone is trying to contain the infection.

Alterations to the apophyseal joints

Degenerative joint disease affecting the apophyseal joints (synovial or facet joints) will lead to typical signs of a degenerative arthritis, that is, loss of joint space and loss of sharpness of apposing joint surfaces due to the deposition of periarticular new bone (Figure 5.35). These joints can be affected by a septic arthritis where the changes will be both destructive and proliferative. The joints may be involved in vertebral neoplasia. Comparison of pairs of these joints on the ventrodorsal view is of value.

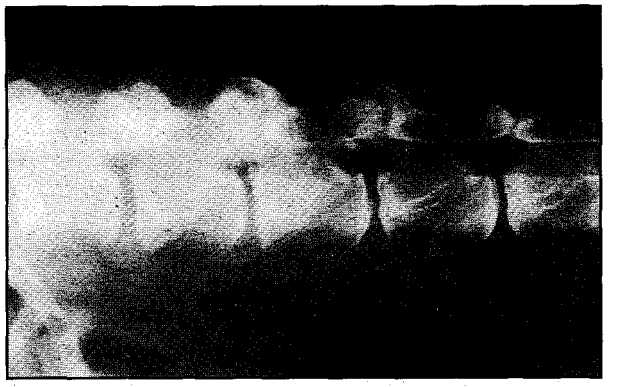


Figure 5.35: Major depositions of new bone and loss of the joint spaces are evident in this case of degenerative joint disease affecting the apophyseal joints in the lumbar spine (vertebral arthritis).

Spinal soft tissue

Unless there is a change in radiographic opacity these tissues are not visible.

Disc anulus fibrosus and nucleus pulposus

Degenerating discs undergo a process leading to mineralisation. This process tends to start in the centre of the nucleus pulposus and radiate outwards. The partially degenerate disc is more vulnerable to deformation than a fully mineralised one. The presence of mineralised disc material often does little more than demonstrate the presence of degenerative disc disease (Figure 5.36). As-yet unopacified or only partially opacified discs warrant the closest scrutiny.

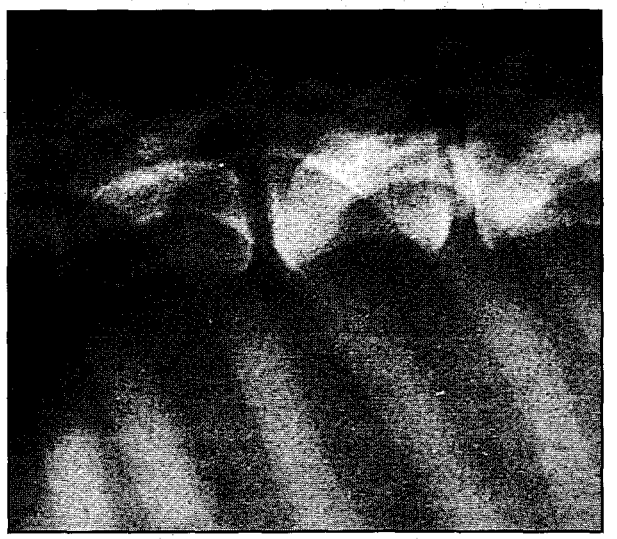


Figure 5.36: A fully mineralised disc is present at T_{12}-T_{13}. It remains in situ and is probably of no clinical significance other than to confirm that the dog has degenerative disc disease.

Spinal cord, meninges and meningeal spaces

Lesions may be extradural, intradural-extramedullary, or intramedullary (Figure 5.37). Their presence can only be determined with the aid of myelography.

Extradural lesions include: intervertebral disc herniation, thickening of the dorsal longitudinal ligament,

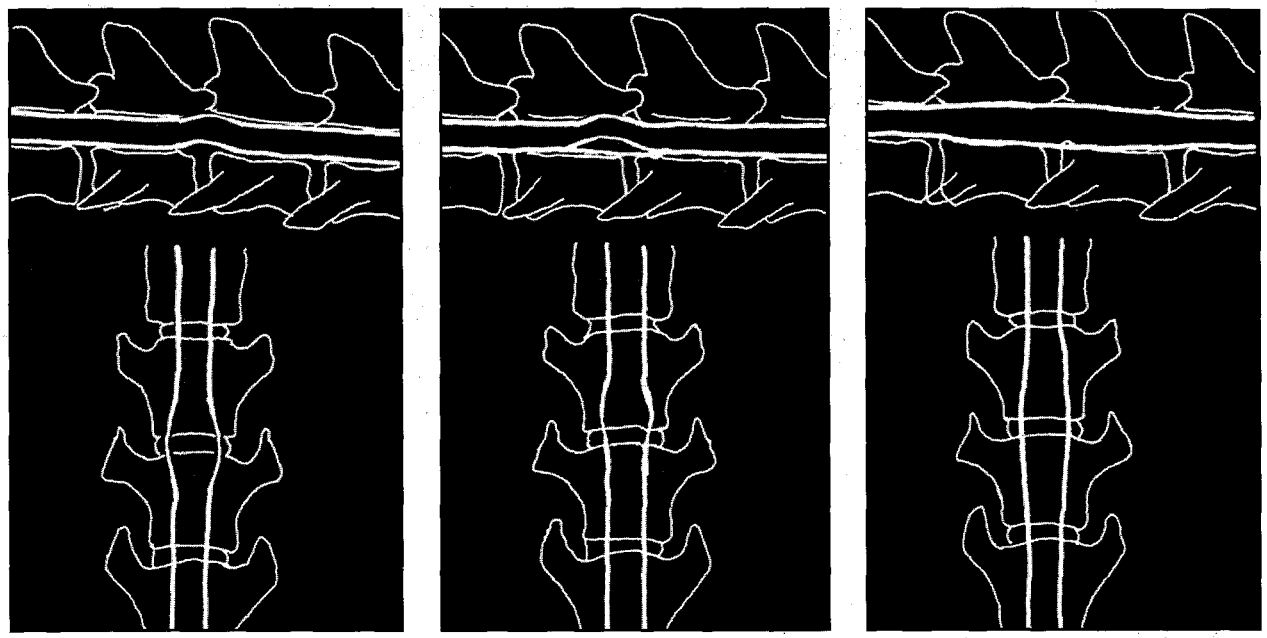


Figure 5.37 (a., b. and c): *Radiolucent lesions that are demonstrated during myelography can be considered as* ***(a)*** *extradural,* ***(b)*** *intradural-extramedullary, or* ***(c)*** *intramedullary.*
(a): *The ventral column is deviated dorsally, the dorsal column is slightly attenuated and, in VD projection, the columns appear to diverge because of the presence of a space occupying lesion ventral to the cord.*
(b): *The presence of an intradural mass is causing the ventral contrast column to bisect and pass either side of it. It is also causing the dorsal column to deviate and in VD projection the columns diverge.*
(c): *An intramedullary mass is causing the contrast columns to diverge in all planes. N.B. The exact location of the lesion around the cord will determine which of the columns is so affected and so two views at right angles are essential for interpretation.*

Figure 5.38: *A massive disc herniation at C_6-C_7 is a good example of an extradural lesion. In this case the herniated disc material is faintly opacified.*

thickening of the ligamentum flavum, haematoma, extradural fat deposits, vertebral body deformation, cervical and lumbosacral spondylopathy, extradural tumours (vertebral, metastases) (Figure 5.38).

Intradural-extramedullary lesions, include: intradural tumours (neurofibroma, meningioma) (Figure 5.39).

Intramedullary lesions include: intramedullary haemorrhage or oedema, intramedullary tumours (ependymoma, astrocytoma) (Figure 5.40). It must be remembered that the normal expansions of the cord at the brachial and lumbosacral outflows mimic intramedullary enlargements.

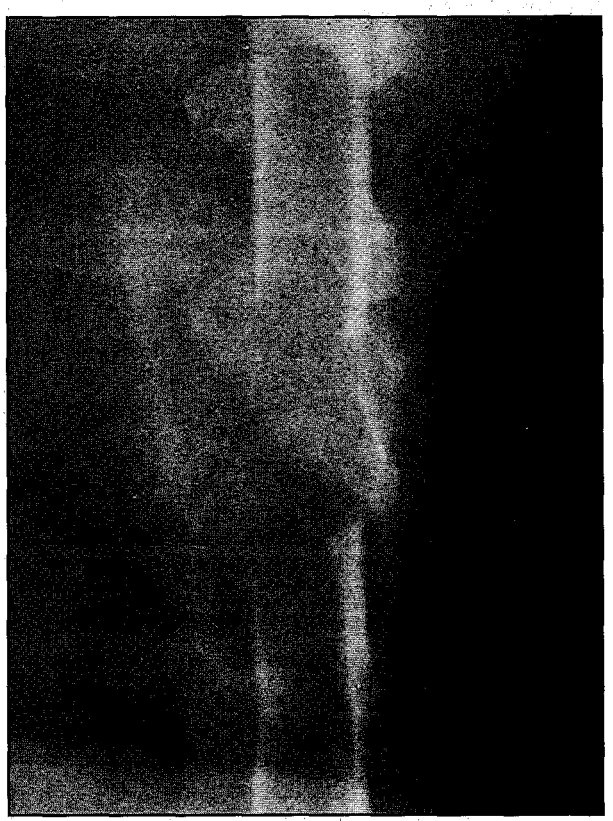


Figure 5.39: *In this case an intradural lesion has caused the subarachnoid space to widen and the accumulation of contrast at this point has caused a classical "golf tee sign". Because of the size of the lesion, the contralateral column has been obliterated but beyond the lesion both columns are restored.*

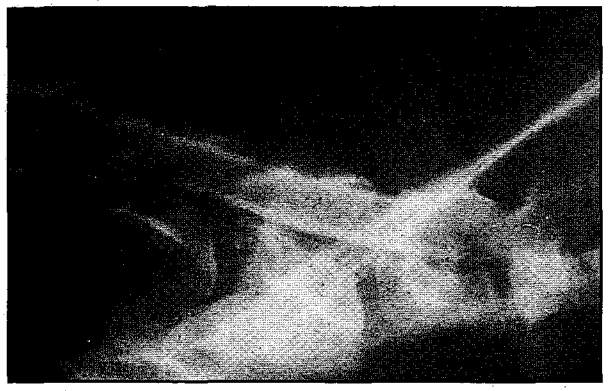


Figure 5.40: An intramedullary mass at the cervicothoracic junction in this dog is causing the contrast columns to diverge, attenuate and finally arrest.

MISCELLANEOUS TECHNIQUES

Portal Venography

Technique

Cases presented with non specific central nervous signs, possibly attributable to hepatic encephalopathy, may require a contrast study to eliminate the possibility of a congenital or acquired venous shunt. Percutaneous splenic injection of contrast is possible. It is said that most humans lose up to one unit of blood following this procedure. In small animals it is most likely that the procedure will be performed under general anaesthesia, and so administration of the contrast via a laparotomy is probable. Again, direct splenic injection is possible and haemorrhage can be monitored and controlled. However, the insertion of a catheter into a mesenteric vein allows repeated injections to be made, particularly if shunt occlusion is to be performed at the same time. The possibility of injecting contrast following partial ligation offers the radiologist / surgeon an accurate means of assessing the success of the procedure.

Portal venography is best carried out on a couch with a fluoroscopic facility. Under general anaesthesia and routine asepsis, a small mid line incision is made just caudal to the umbilicus. Through this a small length of jejunum is delivered and an 18G (1.2 mm) or 20G (0.9mm) catheter inserted into a mesenteric vein and tied in place. A 3-way tap is attached to the catheter. Through this, and via an extension tube to keep the operator's hand out of the primary beam, contrast can be delivered. Three to 10mls of WSCM (300-400 mg I/ml) are delivered as a rapid bolus. If fluoroscopy is available, the timing of the passage of contrast through the portal system can be assessed prior to making spot films. If not, an exposure made just at the end of injection usually will suffice. Whilst in the VD orientation for the laparotomy, it may be possible to determine the presence or absence of a shunt. However, it is usually necessary to make a further injection in lateral recumbency to be sure of the location of the shunt. If a shunt is demonstrated, the laparotomy is extended toward the xiphisternum. It is then worth isolating the vessel and temporarily occluding it with a bulldog clamp. A further injection of contrast will now demonstrate, first, that the correct vessel has been isolated and, secondly, the extent of hepatic vascular architecture. Partial ligation can be performed and further test injections made to evaluate the relative flow through the shunt and the liver. The vessel is usually ligated with silk suture. As a rule of thumb, over-ligation results in the intestines becoming congested and blue. Appropriate ligation seems to be at a point just short of this colour change. Those cases which show a diffuse, branching hepatic vasculature, undoubtedly carry the best prognosis. It is advisable to take a liver biopsy before routine closure of the abdomen.

Radiology of portal venography

Normal vascular anatomy. Blood from the pancreas, spleen and all the gastrointestinal tract, save for the anal canal, reaches the liver via the hepatic portal vein. This accounts for some 80% of the total supply to the liver. Blood is distributed throughout the liver by a system of afferent and efferent vessels. A small supply arrives via the "true" hepatic arteries which are separate from the portal supply. A normal liver venographically will have a diffuse branching system of vessels which extend from the hilus to the periphery in all lobes (Figure 5.41).

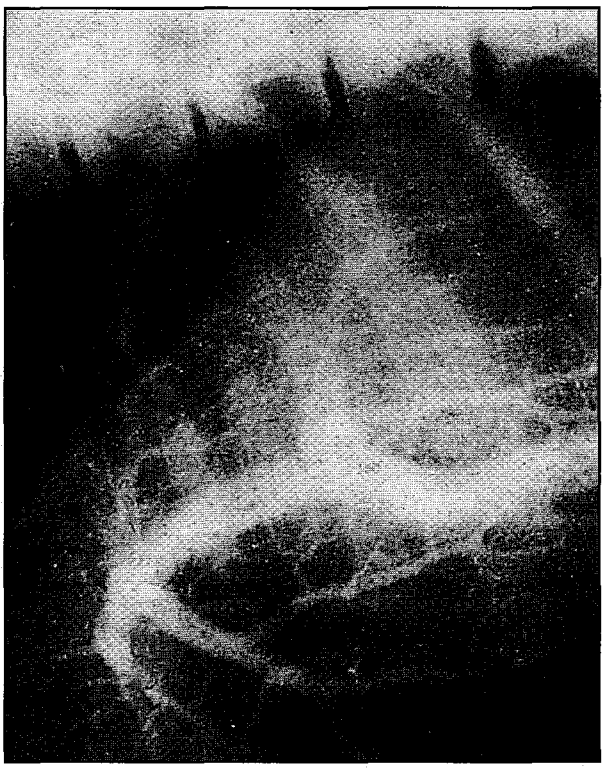


Figure 5.41: A mesenteric vein has been catheterised and water soluble contrast medium administered. The contrast medium is seen to pass via the portal system into normal arboreal pattern of hepatic vessels. Some contrast is just entering the caudal vena cava (normal portohepatic venogram).

Acquired shunts. Acquired shunts occur as a result of portal hypertension usually in response to severe liver disease. They are easily recognised by the proliferation of multitudes of tortuous, anomalous vessels (Figure 5.42).

Figure 5.42: *Contrast is seen to pass via the portal system and into the substance of the liver where a sub-normal arboreal pattern of vessels is present (c.f. Figure 5.41). The caudal vena cava has not yet opacified. An amorphous, tortuous collection of collateral vessels are developing dorsal to the portal vein and extend over the renal shadows towards the spine. These are typical collateral vessels resulting from portal hypertension (acquired shunt).*

Congenital Shunts. These shunts may be extrahepatic (Figure 5.43) or intrahepatic (Figure 5.44) (e/h, i/h) and can occur as follows:

- between the portal inflow and the caval outflow (i/h, right patent ductus venosus or i/h left patent ductus venosus);
- e/h portocaval via the gastroduodenal vein;
- e/h portocaval via the gastrosplenic vein;
- e/h portoazygos via the azygos system.

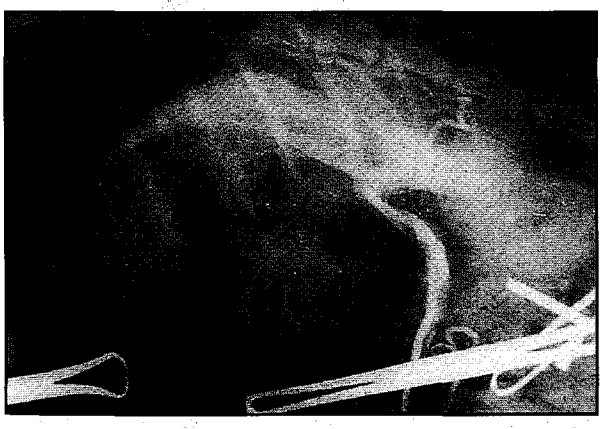


Figure 5.43: *The portal system and hepatic vessels have not opacified. Contrast has shunted directly into the caudal vena cava and the azygos system (congenital extrahepatic shunt).*

The presence of a shunt is easily suspected when the hepatic vessels fail to opacify and contrast is seen to pass directly into the caudal vena cava or azygos system. The precise location of the shunt may be difficult to determine without multiple views. However if ligation is to be attempted under X-ray control then this is not vital.

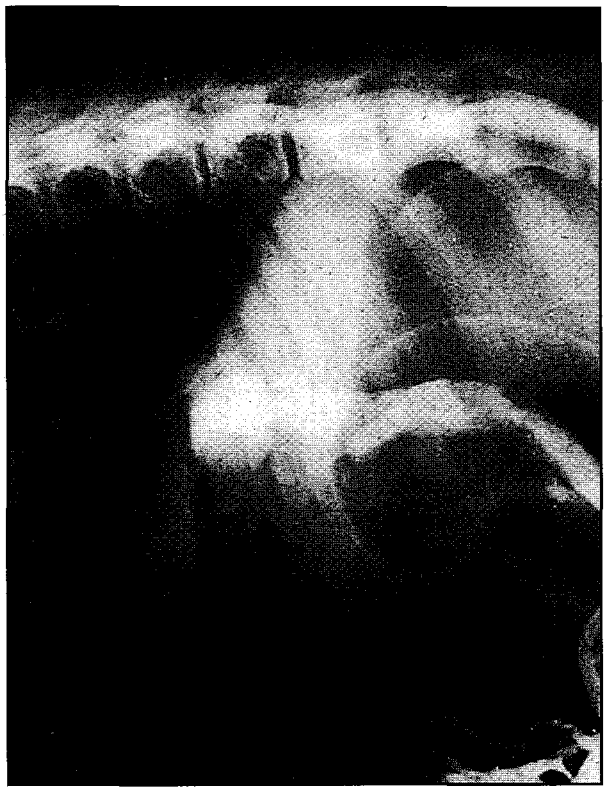


Figure 5.44: *The portal system has opacified as has the caudal vena cava. The hepatic vessels have not opacified. A large connection between the portal vein and the caudal vena cava at the hilus of the liver can be identified (congenital intrahepatic shunt).*

Radiology of Computed Tomography

CT is a useful method for the identification of brain lesions and is now reasonably available in veterinary neurology. This technique is used widely and has been reported extensively in the veterinary literature. Its use has transformed the diagnostic approach to intracranial lesions in all species. Not only will CT scanning identify the presence of a lesion within the brain, but it is possible to make some evaluation of the type of lesion based on the CT characteristics. CT also has a role in the evaluation of the spine in certain circumstances.

Some lesions will be apparent on the plain CT images, but usually the findings of the non-contrast study are restricted to identifying anatomical abnormalities such as hydrocephalus, haemorrhage and the secondary effects of tumours. Brain oedema, deviation of the midline as reflected by displacement of the falx cerebri, and abnormalities of the ventricular system, may be consequences of the presence of a tumour and are termed "mass effect"

Contrast medium administration leads to enhancement of the image of many lesions, because of alterations in the blood-brain barrier, and changes in vascularity with subsequent contrast uptake. Evaluation of CT images is based on the principles of radiology, that is, observation and interpretation of changes in density, shape, position, size, and architecture of the

brain. (Figs 5.45-5.52). Brain scanning in the transverse plain allows comparison of the bilaterally-symmetrical features of anatomy, thus aiding interpretation.

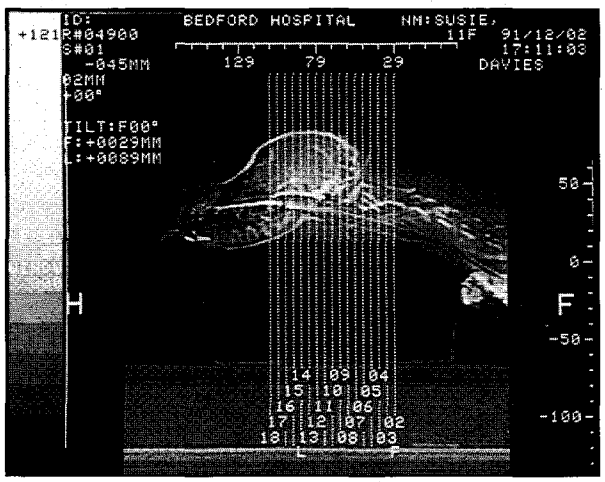


Figure 5.45: *An initial scout film shows a lateral view of the area of interest with the transverse slices marked on it. This can be useful in treatment planning and anatomical orientation.*

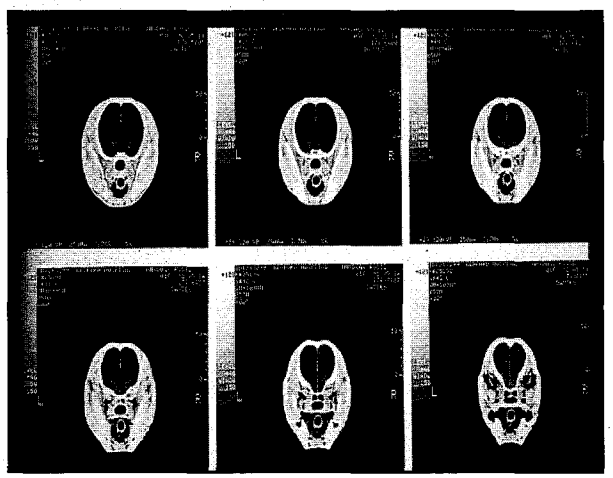


Figure 5.46: *Series of slices from the skull of a Dachshund showing that most of the cranium is occupied by fluid (hyperlucent). Only the mid-line structures and some soft tissue ventrally can be seen in this extreme case of hydrocephalus.*

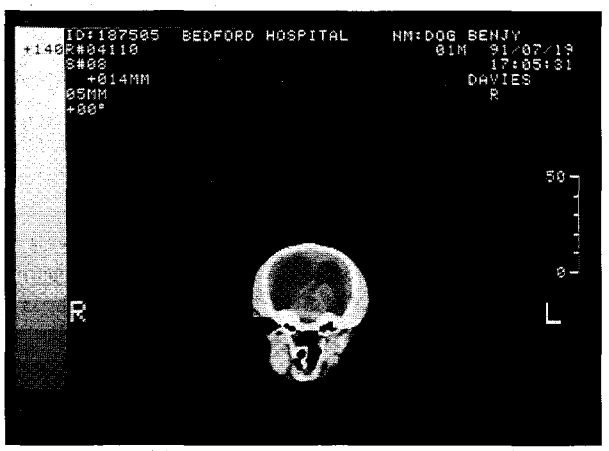


Figure 5.47: *In this crossbred dog the ventricles (lucent) are distended asymmetrically. This animal also has clinical hydrocephalus.*

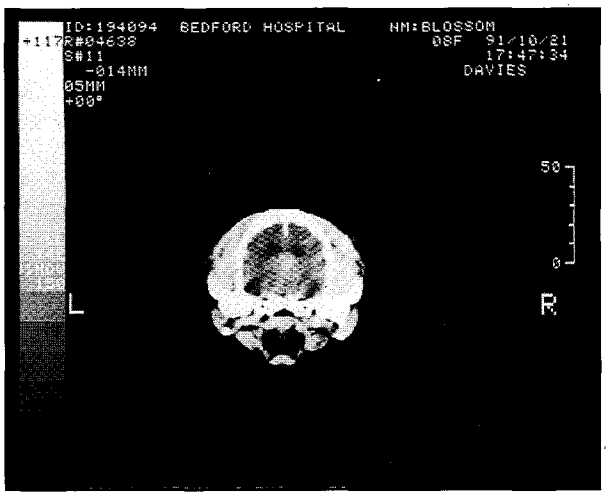


Figure 5.48a: *This dog has a roughly circular area of increased attenuation in the midline immediately ventral to the lateral ventricles (lucent). Note the almost tartan-like streak artefacts affecting the image.*

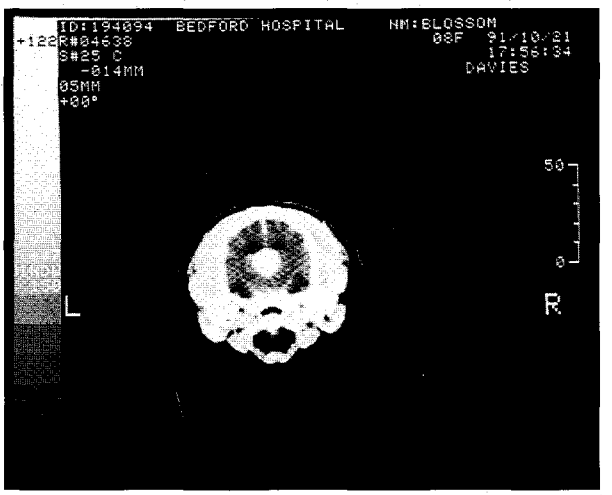


Figure 5.48b : *Following the administration of intravenous contrast there has been intense enhancement of the circular lesion ventral to the ventricles that was seen on the same slice before contrast (Figure 5.47a). This was a pineal body tumour.*

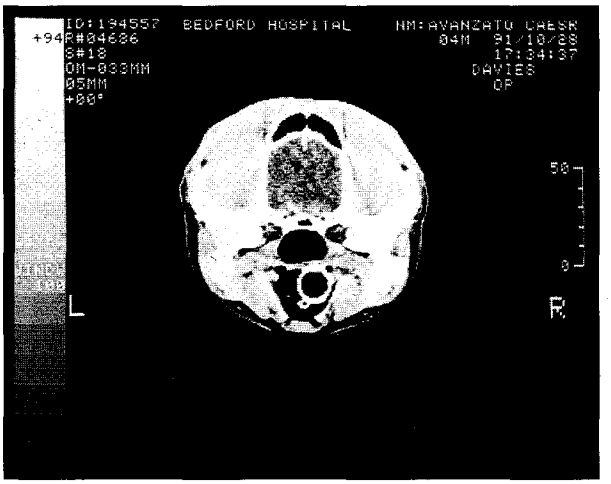


Figure 5.49a : *This Boxer had been confirmed as having both adrenal and thyroid dysfunction and then developed CNS signs. The pre-contrast slice is unremarkable save for streak artefact.*

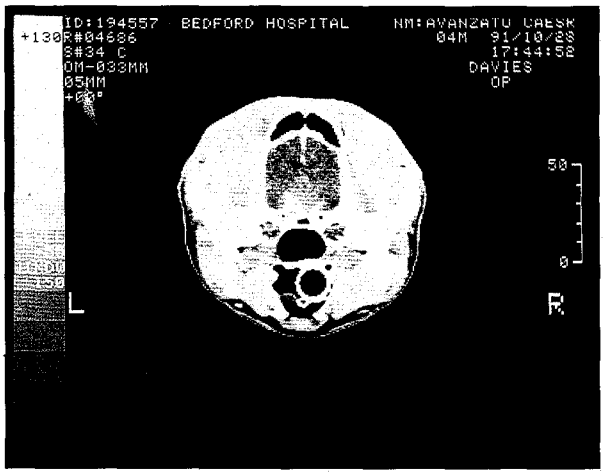


Figure 5.49b : *Following intravenous contrast enhancement an amorphous mass can be seen in the hypothalamic area dorsal to the pituitary. This tumour had extended from the pituitary into the hypothalamus.*

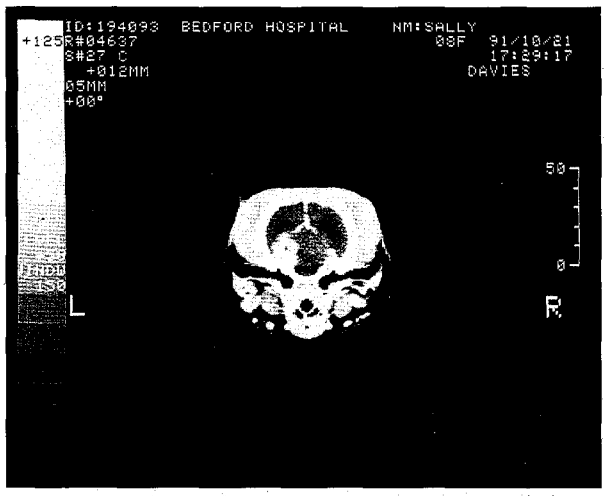


Figure 5.50 : *The intensely enhancing and well marginated peripheral lesion just ventrolateral to the tentorium cerebelli is a typical meningioma.*

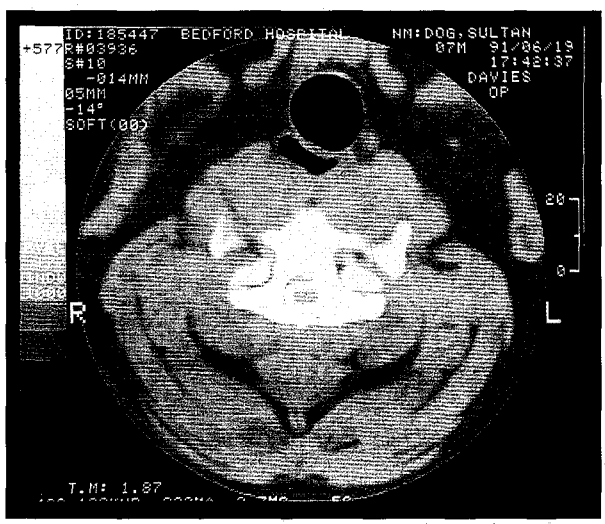


Figure 5.51a: *These slices (ventrodorsal recumbency) are from the cervical spine of a Dobermann with cervical spondylopathy following the administration of a low dose of intrathecal contrast. This slice #10 is through the C_7-T_1 disc space. Note the heads of the first ribs that are showing. The thecal sac is a perfect ellipse around the spinal cord.*

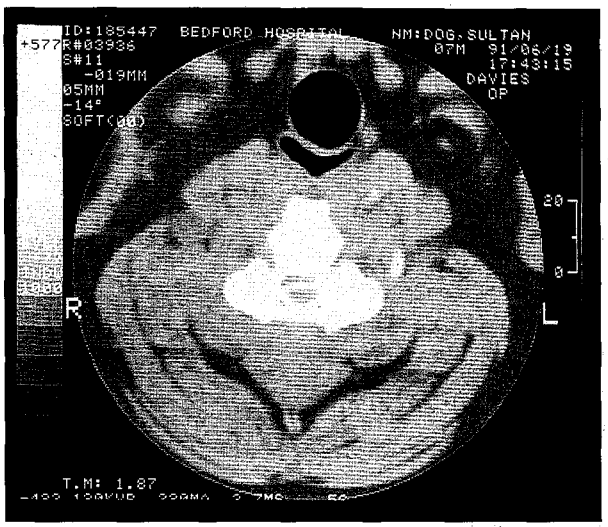


Figure 5.51b : *The next slice #11 is through mid-C_7 and shows displacement of the thecal sac ventrolaterally on the right of the patient. This has been caused by prolapsed disc material that has extruded caudally from the C_6-C_7 disc space.*

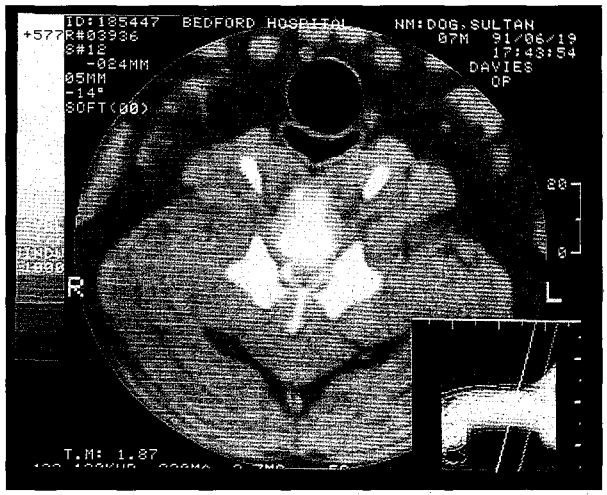


Figure 5.51c: *The next slice #12 is right through the C_6-C_7 disc space. Note the tips of the long transverse processes of C_6 and the intervertebral foraminae, which are visible.*

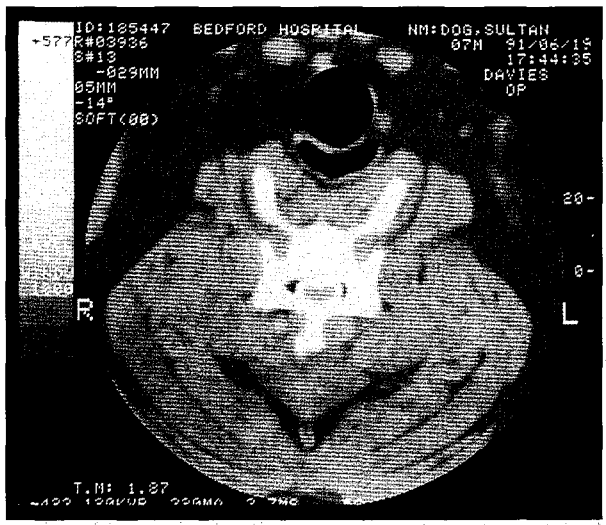


Figure 5.51d: *The next slice #13 is through mid C_6. Note the very dorsoventrally flattened shape of the vertebral canal compared to slice #10, although the thecal sac is not compromised.*

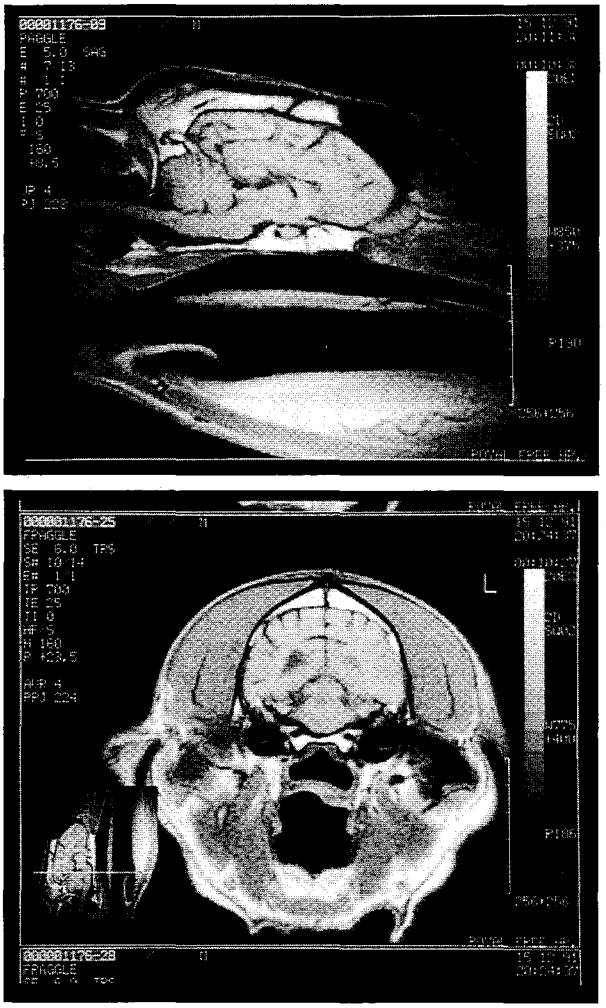


Figure 5.52 (a and b): *Sagittal and transverse sections through the brain of an Italian Spinone with cerebellar and cerebral hypoplasia. Members of the same litter were variously affected. These T1-weighted images give exquisite detail of the CNS. The CSF indentations (black, hypointense) surrounding the cerebellum and the remainder of the brain were wider and deeper in the more affected individuals.*

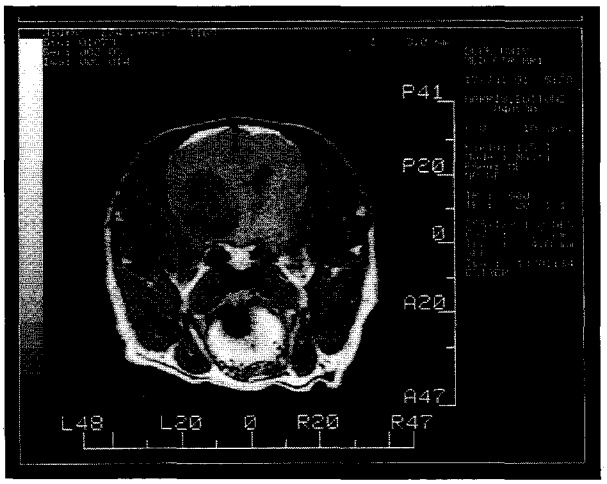


Figure 53: *MRI of a Poodle with a glioma.*
(a:) *T1-weighted image shows hypointense area in the left forebrain. Note also the hypointense (black) CSF in the right lateral ventricle, and that the left lateral ventricle is not visible.*

Radiology of Magnetic Resonance Imaging

The principles of radiological interpretation should also be applied to MRI images in terms of the changes in position, size etc. However the opacity of different tissue types is quite different and alters depending upon the type of MRI image being examined (i.e. T1-weighted, T2-weighted, contrast enhanced) (Figure 5.53).

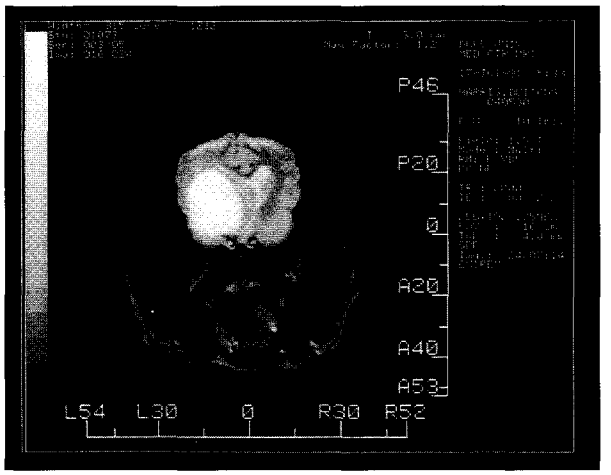


Figure 5.53: *MRI of a Poodle with a glioma.*
(b:) *T2-weighted image shows the lesion as being uniformly hypointense. The CSF in the right lateral ventricle is also hypointense (white).*

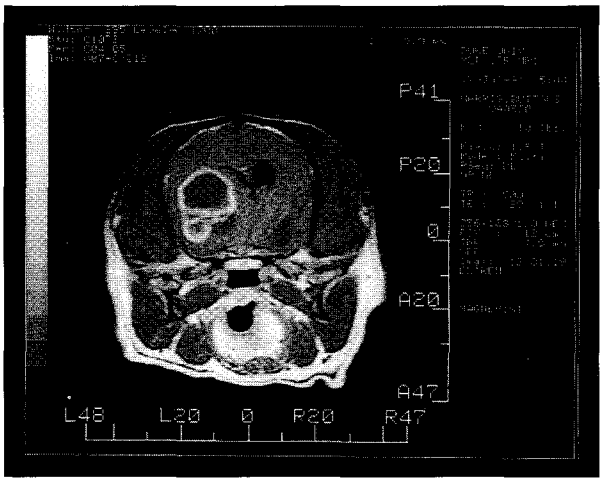


Figure 5.53: *MRI of a Poodle with a glioma.*
(c:) *T1-weighted, gadolinium-enhanced image shows that only the periphery of the lesion takes up contrast. At surgery, the lesion proved to be cystic.*

ACKNOWLEDGEMENTS

Figure 5.51a, 5.51b, 5.51c and 5.51d form part of a study funded by the BSAVA CSTF.

FURTHER READING

Carlton RR and McKenna Adler A (1992) *Principles of Radiographic Imaging - An art and a science.* Delmar Publishers Inc., New York.

CHAPTER SIX

Clinical Pharmacology and Therapeutics of the Nervous System

Peter M. Keen

PART 1 - CLASSIFICATION OF DRUGS BY MODE OF ACTION

An understanding of mechanisms of drug action is necessary to appreciate the effects, uses and interactions of the various drugs dealt with in Part II of this chapter. These drugs act almost exclusively through the various neurotransmitter systems of the brain. Because of the functional complexity of these systems, this account must necessarily involve considerable generalisation and the reader is referred to the texts listed under Further Reading for a more detailed treatment.

The following mechanisms of action are discussed:

- **A. Drugs Interacting with the Noradrenaline System**
- **B. Drugs Interacting with the Dopamine System**
- **C. Drugs Interacting with Inhibatory Amino Acids**
- **D. Drugs Interacting with the 5-Hydroxytryptamine (Serotonin) System**
- **E. Drugs Interacting with the Opioid System**
- **F. Drugs Interacting with the Excitatory Amino Acids**
- **G. Drugs that Interact with the Sodium Channels**

A. Drugs Interacting with the Noradrenaline System

The functions of the noradrenaline system include regulation of mood, arousal and blood pressure.

Drugs that activate the noradrenaline system

a. Release noradrenaline. Amphetamine releases noradrenaline and also 5-hydroxytryptamine (5HT) and dopamine. It is thus a psychomotor stimulant and is dealt with below.

b. Inhibit noradrenaline inactivation. Tricyclic antidepressants such as amitriptyline, inhibit re-uptake of noradrenaline into nerve endings, while monoamine oxidase inhibitors such as tranylcypromine delay breakdown of noradrenaline and so each in its own way increases the concentration of noradrenaline in the synaptic cleft thus causing arousal and elevation of mood. These drugs are hence known as antidepressants.

Drugs that inhibit the noradrenaline system

a. α_2 stimulants Xylazine, detomidine and medetomidine selectively activate the α_2 receptors, through which noradrenaline inhibits its own release and thus produce sedation, analgesia and a fall in blood pressure. Atipamezole selectively blocks these α_2 receptors and so may be used to antagonise the action of α_2 stimulants.

b. ß-blockers. Propranolol blocks the action of noradrenaline at ß-receptors and so reduces tension and produces a fall of blood pressure, the latter by its actions in the peripheral nervous system.

B. Drugs Interacting with the Dopamine System

The functions of the dopamine system include regulation of motor activity (through the extrapyramidal system), behaviour (through the mesolimbic system), vomiting (at the chemoreceptor trigger zone), and prolactin secretion (through the tubero-infundibular system).

Prolactin secretion

Dopamine inhibits secretion of prolactin from the lactotrophes of the anterior pituitary gland. Thus drugs such as bromocriptine (Parlodel®), which stimulate dopamine receptors reduce prolactin secretion and are used to treat pseudopregnancy.

Conversely, the phenothiazine tranquillisers such as acepromazine (see below), which are dopamine antagonists, are contraindicated in pseudopregnancy.

Vomiting

Dopamine is an excitatory neurotransmitter in the vomiting pathway. Apomorphine stimulates these

dopamine receptors and is a powerful emetic, and conversely the dopamine antagonist metoclopramide (Emequell®) is used as an antiemetic. (Dopamine inhibits gastric motility and so metoclopramide also decreases gastric emptying time by a peripheral action.)

Acepromazine

Acepromazine, thioridazine and other phenothiazine tranquillisers are dopamine antagonists and are classed as neuroleptics or major tranquillisers. They lower reactivity to external stimuli, modify behaviour, are antiemetic and increase prolactin secretion. Prolonged use in man may give rise to motor dysfunction (tardive dyskinesia) characterised by involuntary movements.

Amphetamines

Dexamphetamine (now a Controlled Drug) releases noradrenaline and dopamine and so increases motor activity, produces wakefulness, psychic stimulation and anorexia and is classed as a psychomotor stimulant.

C. Drugs Interacting with Inhibitory Amino Acids

1. GABA (Gamma-aminobutyric acid)

GABA, the chief inhibitory neurotransmitter, is contained in short inhibitory neurones throughout the brain.

Drugs that activate the GABA system. The GABA receptor is closely linked to a chloride channel in the neuronal membrane. Occupation of the receptor opens the chloride channel, which inhibits cell firing.

Benzodiazepines potentiate GABA by facilitating its binding to the receptor. Thus members of the group are to varying degrees sedative, anticonvulsant and reduce anxiety and aggression. They also stimulate appetite. They are known as anxiolytic sedatives or minor tranquillisers.

Barbiturates also facilitate the bonding of GABA to its receptor, although the relevance of this to their overall depressant effects is not clear.

Sodium valproate is anticonvulsant by virtue of its ability to inhibit GABA breakdown.

Ivermectin activates the GABA system by releasing GABA from nerve terminals. Mammals, unlike the parasites on which ivermectin acts, do not use GABA as a neurotransmitter in their peripheral nervous system and ivermectin is unable to enter the brain. Hence, ivermectin does not normally produce nervous effects in mammals. In Collie dogs, however, the blood-brain barrier is permeable to the drug so that unlicensed use of ivermectin in these animals may lead to severe and particularly prolonged CNS depression.

Drugs that oppose the GABA system. Picrotoxin combines directly with the GABA-controlled chloride channel, which it closes thus opposing the effect of GABA.

Picrotoxin is thus a general CNS stimulant. When used to stimulate respiration it may cause convulsions and so has been superseded by the safer doxapram. Picrotoxin has been used to treat ivermectin overdose.

2. Glycine

Glycine is an inhibitory neurotransmitter in the spinal cord. Strychnine is a glycine antagonist and so causes enhancement of spinal reflexes, and, in high doses, spinal convulsions.

D. Drugs Interacting with the 5-Hydroxytryptamine (Serotonin) System

5-HT neurones play a role in mood and anxiety, vomiting, nociception and, through regulating the release of other neurotransmitters, have many other actions.

There are a range of 5HT receptor subtypes and drugs are being developed to interact more or less selectively with these.

Buspirone, a 5HT1a agonist is a non-sedative anxiolytic used in anxiety states as a non-sedative alternative to the benzodiazepines, but has a long latent period to onset of action.

Ondansetron is a 5HT3 antagonist which is a potent central antiemetic.

Fluoxetine increases 5HT activity by specifically blocking 5HT uptake and shares some properties with the trycyclic antidepressants such as amytriptyline, which blocks both 5HT and noradrenaline uptake. It is used in stereotypy and aggression.

E. Drugs Interacting with the Opioid System

The opiate analgesics interact with the receptors for a range of endogenous opioid peptides including the endorphins, the enkephalins and dynorphin. Acting through the mu receptor, morphine gives analgesia and cough suppression, but also respiratory depression and physical dependence. More recently-developed agents such as butorphanol and the longer-lasting buprenorphine act partly at least through kappa receptors and so produce less respiratory depression and physical dependence than morphine. Butorphanol is analgesic and antitussive. Buprenorphine is analgesic and a partial agonist so that its effects are only partly reversed by naloxone.

The opioid antagonists naloxone and naltrexone may find application in the treatment of obsessive, stereotypic behaviours.

F. Drugs Interacting with the Excitatory Amino Acids

The amino acid glutamate, or a closely-related substance, is thought to function as a widespread excitatory

transmitter in the brain and spinal cord. The dissociative anaesthetics such as ketamine block one class of glutamate receptor, the NMDA receptor. Other NMDA antagonists may find application in the treatment of epilepsy and in the prevention of ischaemic brain damage.

G. Drugs that Interact with the Sodium Channels

Some drugs act, not through neurotransmitter systems, but directly through the sodium conductance channels of neuronal membranes which open during cell firing.

1. Drugs that block sodium channels

Lignocaine acts as a local anaesthetic by blocking sodium conductance channels and the same mechanism accounts for its anticonvulsant activity (and its anti-arrhythmic activity in the myocardium).

Phenytoin also blocks sodium channels but only during rapid firing. It thus suppresses the spread from an epileptic focus but has relatively little effect on normal cortical function and so it is less sedative than other anticonvulsants such as the barbiturates.

2. Drugs that open sodium channels.

The chlorinated hydrocarbon insecticides (e.g. Gammexane®) and also pyrethroids (e.g. cypermethrin) act to prolong the opening of sodium conductance channels and so cause CNS excitement in overdose.

PART II - USE OF DRUGS IN SPECIFIC CONDITIONS

The following conditions are discussed:

- **Seizures**
- **Vomiting**
- **Behavioural Disorders**
- **Acute Trauma to Brain and Spinal Cord**
- **Intervertrbal Disc Herniation**
- **Heat Stroke**
- **Narcolepsy**
- **Hepatic Encephalopathy**
- **Infections of the Central Nervous System**
- **Granulomatous Meningoencephalomyelitis (Primary Reticulosis)**

Seizures

Status epilepticus

Convulsions are best controlled by intravenous injection of a benzodiazepine. Diazepam (Valium®) 0.25 - 1.0 mg/kg intravenously (IV) is most commonly employed but it is rapidly redistributed following IV injection and has a short half-life of elimination (Table 6.1) and so may require repeated injection. An alternative is clonazepam (Rivotril®) 0.05 - 0.2 mg/kg slowly IV.

If benzodiazepines fail to control the convulsions, recourse must be made to the barbiturates. Phenobarbitone is available in injectable form (Phenobar-

*Table 6.1: Elimination half-lives of anticonvulsants in the dog**

Generic Name	Brand name	Half-life (hours)
Diazepam	Valium	2 - 5
Phenobarbitone	Gardenal, Luminal	64
Primidone	Mysoline	9 - 12**
Phenytoin	Epanutin	4.5
Ethosuximide	Zarontin	17
Carbamazepine	Tegretol	1 - 2
Sodium valproate	Epilim	2

* Data adapted from Frey & Loscher (1985) and Frey (1986)
** Half-life is of parent drug which is metabolised to phenobarbitone (see text)

bitone Injection; Gardenal Sodium®), 2 - 4 mg/kg IV, but has a long latency of effect and is slowly eliminated (Table 6.1). Alternatively, pentobarbitone can be used, 4 - 20 mg/kg IV to effect, although this is a less selective anticonvulsant than phenobarbitone and so may cause considerable sedation.

Generalised tonic/clonic seizures (grand mal)

Therapeutic principles.

The overall aim of therapy is to control the seizures with a minimum of sedation. For this reason, if medication is given once daily, it should be given in the evening.

A pre-requisite of successful therapy is to maintain a constant concentration of the drug in the body. For this we require drugs with relatively long half-lives of elimination.

A rapidly-eliminated drug requires frequent administration and is likely to produce unacceptable fluctuations in blood concentrations.

Anticonvulsant drugs need to be administered over considerable periods of time and this introduces a number of complications:

- If a constant dose is given at regular intervals the drug will accumulate in the body. As a rule of thumb, if a dose is administered at intervals of one half-life, then plateau concentrations will be reached after five half-lives (see Table 6.1 for representative half-lives). Note that a similar period will elapse between changing the dose of a drug and stabilisation at the new concentration.
- Many anticonvulsant drugs induce the hepatic microsomal enzyme systems, which are responsible for their metabolism. Thus, after a period of continuous medication, the animal will become tolerant not only to the drug itself but also to other drugs metabolised by the same pathway. Phenobarbitone and phenytoin show cross tolerance of this kind.
- The longer a drug is given the more likely it is to cause long-term adverse effects.

During treatment care must be taken not to precipitate status epilepticus in any of the following ways:

- by abruptly withdrawing medication
- by abruptly changing from one drug to another; the effect of the first may be lost before that of the second is established.

Acepromazine, chlorpromazine and other dopamine antagonists should be avoided as they may precipitate seizures in a susceptible animal.

Chloramphenicol should also be avoided because it inhibits the hepatic microsomal enzymes, greatly enhancing the effect of those anticonvulsants which are metabolised by this route.

Drugs used

a. Phenobarbitone (Gardenal®, Luminal®). Phenobarbitone is the drug of choice for the long-term control of generalised seizures in both the dog and cat. It acts to suppress spontaneous discharges with little effect on spread to other areas. In the naive animal phenobarbitone is slowly eliminated, partly by hepatic metabolism and partly through renal excretion of unchanged drug. The initial oral dose in the dog is 1.5 - 2.5 mg/kg twice daily (BID) and in the cat 0.5 - 1.5 mg/kg twice daily (BID) This dose may initially cause sedation and ataxia but these effects soon disappear due to development of tolerance, and the dose may then have to be increased several-fold bearing in mind that following each change in dosage a period of more than a week must elapse before the drug reaches its new plateau. It is hoped that in this way control of seizures may be achieved without an unacceptable degree of sedation/ataxia.

Phenobarbitone may give rise to a number of minor side-effects including polyphagia, polydipsia and polyuria (the latter due to inhibition of ADH release). It has also been reported to cause whining in toy breeds.

b. Primidone (Mysoline®). Primidone would seem to carry no advantages over phenobarbitone to which it is, in fact, metabolised and to which its effect is almost entirely due. Moreover, primidone is potentially more toxic than phenobarbitone. Primidone itself has anticonvulsant activity and is broken down in the liver to phenobarbitone and a second metabolite PEMA, which is relatively inactive and hepatotoxic. Since the half-life of phenobarbitone is much longer than that of primidone (see Table 6.1) it accumulates, so that when steady state conditions are reached 14 days after initiation of therapy, plasma concentrations of phenobarbitone are nearly five fold higher than those of primidone, so that 85% of anticonvulsant activity can be attributed to the phenobarbitone.

In the dog, primidone is initially given at 15-30 mg/kg orally daily in two or three divided doses, increasing to 30-50 mg/kg daily as tolerance develops. Primidone is not suitable for use in the cat because conversion to phenobarbitone is much less efficient than in the dog. As is to be expected, primidone, like phenobarbitone, may produce sedation/ataxia, polyphagia, polydipsia and polyuria. It may also, however, cause liver damage, a problem not encountered with phenobarbitone.

c. Phenytoin (Epanutin®). Unlike barbiturates, which act to suppress the epileptic focus, phenytoin stabilises membranes and so prevents the spread of seizure activity. As a result of this different mechanism of action, phenytoin is less sedative than phenobarbitone. It is broken down by the same hepatic enzyme that metabolises phenobarbitone and is a potent inducer of this enzyme.

The major limitation of phenytoin is its very short half-life (Table 6.1). Doses as high as 35 mg/kg three times daily (TID) orally must be given to attain therapeutic concentrations in plasma and this makes it unsuitable for use as an anticonvulsant in the dog. A sustained-release preparation has recently been developed, which may overcome this problem.

Reports of phenytoin toxicity in the dog are rare, possibly because of the low plasma concentrations normally achieved. Potential toxic effects are: hepatic insufficiency, conditioned folate deficiency (phenytoin induces the enzyme which breaks down folate) leading to megaloblastic anaemia, and gingival hyperplasia.

Phenytoin is more slowly metabolised in the cat than in the dog (half-life 24-108 hours) and so may be given at 2 - 3 mg/kg/daily orally, but accumulation to toxic concentrations, heralded by sedation, ataxia and anorexia, may occur.

d. Potassium Bromide. Potassium bromide (10 - 15 mg/kg twice daily) may be used as an adjunct to phenobarbitone when satisfactory control is not otherwise achieved.

e. Benzodiazepines. Diazepam is too short-acting but the longer lasting clonazepam or chlordiazepoxide can be used, although tolerance to their anticonvulsant action is likely to develop with time.

f. Other Drugs. Carbamazepine (Tegretol®) and sodium valproate (Epilim®) are not suitable for long-term control of seizures owing to their very short half lives (Table 6.1). Ethosuximide (Zarontin®) has been used in man for absence seizures (petit mal) but this condition occurs only rarely in the dog or cat.

Vomiting

Drugs used

Emetics. Apart from local emetics (Ipecacuanha®, washing soda etc.) the α_2 agonist xylazine may be given intravenously at 0.2 mg/kg to cause vomiting at which dose it is unlikely to cause undue sedation.

Antiemetics. These include:

- Metoclopramide - a dopamine antagonist
- Acepromazine and other phenothiazine tranquillisers
- Ondansetron - a 5HT3 antagonist

Behavioural Disorders

Drugs used

Progestagens. The progestagens, megoestrol acetate and medroxyprogesterone acetate act via the hypothalamus to reduce gonadotrophin secretion and hence reduce testosterone concentrations. They thus find their chief application in those behavioural disorders which are related to male sexual drive. In addition they, and particularly megoestrol, act directly on the CNS to influence mood and generally tractability and so also find application in a number of stress-related disorders.

The toxicity of progestagens given over a period of time is by no means negligible. They may cause hyperglycaemia, glucose intolerance and raised growth hormone concentrations - the so-called diabetes/acromegaly syndrome . They may also cause polydipsia, polyuria and polyphagia leading to increased weight gain. More rarely, progestagens may cause mammary hyperplasia.

Megoestrol acetate is given by regular oral administration. Medroxyprogesterone acetate is given intramuscularly (IM) or subcutaneously (SC) as a repository injection. Dosage rates are:-

Megoestrol acetate: Dog: initially 2 mg/kg per day orally for two weeks, gradually reducing the dosage thereafter. If no response after a further week the dose may be briefly increased to 4 mg/kg/day. Cat: 2 mg/kg daily orally for 1-3 weeks, reducing the dose thereafter.

Medroxyprogesterone acetate: Dog: 10-20 mg/kg IM or SC every 3-6 months. Cat: 10 mg/kg every 3-6 months.

In general, megoestrol is preferred to medroxyprogesterone for most behavioural conditions because of its greater direct effect on the brain and the fact that oral administration allows the dosage to be more accurately controlled.

Minor tranquillisers. Minor tranquillisers such as the benzodiazepines diazepam (Valium®) and nitrazepam (Mogadon®) find application in a number of behavioural disorders including phobias (e.g. thunderstorms), anorexia and spraying in cats.

They may also be used to reduce sexual drive while progestagens are taking effect. By reducing fear benzodiazepines may increase aggressiveness. Dosage rate is 0.25 mg/kg three times daily (TID) in both dogs and cats.

An alternative to the benzodiazepines is the non-sedative buspirone, a 5HT1a agonist.

Anti-anxiety drugs. The tricyclic antidepressant amitriptyline, 1-2 mg/kg orally daily, may be used to reduce the anxiety which underlies behavioural disorders such as excessive grooming in cats and separation anxiety in dogs.

Psychomotor stimulants. Paradoxically, low doses of the psychomotor stimulant dexamphetamine (Dexedrine®) are effective in hyperkinesis in dogs. Care must be taken not to give an overdose which may cause hyperactivity and stereotypic (repeated, pointless) behaviour. Dose in dogs is 0.2 - 1.3 mg/kg orally daily.

Major tranquillisers. Major tranquillisers such as chlorpromazine, so called because they are effective in a range of human psychoses, reduce reactivity to external cues and so find little application in the therapy of behavioural conditions in dogs and cats.

Classification of conditions by preferred therapy

Class 1. Related to male sex drive hence progestagens are first choice. Benzodiazepines are reserved for use if progestagens fail to suppress signs while progestagens are taking effect.

- Aggression
- Urine-marking
- Mounting
- Sexual perversion
- Roaming
- Spraying

In the last case benzodiazepines may be preferred.

Class 2. Stress-related conditions in which benzodiazepines or buspirone are the agents of first choice and progestagens second choice.

- Phobias
- Anorexia

Class 3. Anxiety-related syndromes in which amitriptyline is first choice and progestagens are used if this fails.

- Excessive grooming
- Separation anxiety

Class 4. Hyperkinetic syndromes in which dexamphetamine is specifically indicated.

Class 5. Compulsive and obsessive behaviours in which opiate antagonists (naxloxone and naltrexone) are indicated.

Acute Trauma to Brain and Spinal Cord

Brain trauma

Corticosteroids are widely accepted as the standard treatment for brain trauma, their chief effect being to reduce brain oedema. If, depending on the circumstances of the case, shock is present then large doses of corticosteroids (e.g. 2.5 mg/kg dexamethasone IV TID for two days) are usually given. If the animal is not in shock then lower doses of corticosteroids (e.g. 0.25 mg/kg dexamethasone IV) should be given to reduce brain oedema while avoiding the side effects of larger doses of corticosteroids.

Fluid intake should be restricted to minimise oedema.

The osmotic diuretic mannitol (Osmitrol®) 1 - 2 g/kg IV every 4-6 hours for three days has also been given to reduce oedema, although recent work suggests that doses of 0.25 g/kg may reduce intracranial pressure while avoiding the risks of severe dehydration and renal dysfunction. Mannitol should not be used if there is hypovolaemic shock or ongoing haemorrhage.

Blunt trauma to spinal cord

A great deal of experimental work has been done on mechanisms of nervous tissue damage in blunt injury to the spinal cord. Briefly, it seems that apart from the initial direct damage to spinal cord pathways caused by the trauma, there are also indirect mechanisms whereby mediators released from damaged cells cause secondary cellular damage and reduce spinal cord blood flow, which in turn causes ischaemic necrosis. Currently, the number of postulated mechanisms is matched by an equal number of suggested remedies.

Corticosteroids are the treatment of choice for spinal cord trauma and have been shown to improve spinal cord blood flow and increase functional recovery. One trial showed that soluble corticosteroid (in this case methylprednisolone sodium succinate) produced best results. The suggested dosage regime is an initial IV bolus of 30 mg/kg methylprednisolone, followed by 15 mg/kg IV 2 and 6 hours later, then 2.5 mg/kg IV per hour for a further 24-48 hours (Brown and Hall 1992). A major consideration when using corticosteroids in spinal cord trauma is that both corticosteroids and trauma to the spinal cord may separately lead to gastrointestinal ulceration so that a combination of the two is particularly dangerous in this respect. For instance, corticosteroids have caused fatal colonic perforation in dogs undergoing surgery for intervertebral disc protrusion.

Oedema does not play a major part in the reaction of the spinal cord to trauma and so, in contrast to trauma of the brain, there is no place for osmotic diuretics such as mannitol in the management of this condition.

Intervertebral Disc Herniation

With severe pain

Prednisolone 0.5 mg/kg orally BID for 72 hours reduces inflammation of nerve roots, increases blood flow and hence reduces pain. The risk of gastrointestinal ulceration mentioned above should be borne in mind. This is highly likely to happen if corticosteroids are given in combination with non-steroidal, anti-inflammatory agents. Thus, these drugs should never be given in combination. The relief of pain may make the patient more active, which can lead to a precipitous worsening of the neurological status. Thus, anti-inflammatory drugs should only be given to patients that are confined to a small cage, preventing movement.

With total paralysis
Methylprednisolone sodium succinate as described above for spinal trauma may improve the prognosis.

Heat Stroke

The priority must be to reduce body temperature. This is best done by total body immersion in cold water. Antipyretic analgesics are not indicated since the thermoregulatory centre is not the source of the hyperthermia. Glucocorticoids or mannitol (see Brain Trauma above) may be used to reduce cerebral oedema.

Narcolepsy

Agents of choice in this condition are the psychomotor stimulants (see above).

Dexamphetamine (Dexedrine®) 0.2 - 1.3 mg/kg daily orally may be used. This is now classified as a Controlled Drug. An alternative is the tricyclic antidepressant imipramine (Tofranil®) 0.5 - 1.0 mg/kg daily orally. This may take some time to establish its effect and should not be suddenly withdrawn. Monoamine oxidase inhibitors are contraindicated.

Hepatic Encephalopathy

Aetiology
Hepatic encephalopathy occurs in advanced liver disease and/or portal systemic shunting, and is largely due to failure of the diseased liver to remove toxic products of gut metabolism from the portal circulation. These toxic products include:

Ammonia produced by bacteria in the colon would normally be converted to urea in the liver. This no longer occurs and so plasma ammonia rises, plasma urea falls and ammonium biurate crystals may be formed in the urine. Dietary protein is a substrate for ammonia-producing bacteria and so exacerbates the condition.

Amino acids. There is a rise in plasma aromatic amino acids (tyrosine, phenylalanine, tryptophan), which are normally metabolised in the liver. These may enter the brain to interfere with amine neurotransmitter mechanisms.

There is a concurrent fall in branched-chain amino acids (valine, leucine, isoleucine) which are metabolised in muscle rather than in liver and, as these compete with aromatic amino acids for uptake into the brain, the uptake of the latter into brain tissue is further increased.

Plasma concentrations of mercaptans, which are produced by gut bacteria from methionine, also increase and may enter the brain. One of the mercaptans, dimethyl sulphide, gives the breath its characteristic odour.

Treatment
Cease protein intake, as dietary protein is the major source of ammonia.

Empty the colon by an enema or cathartic. This removes colonic bacteria and their products.

Lactulose (Duphalac®) 5 - 15 mls orally TID daily. Lactulose is a semisynthetic disaccharide which is split by gut bacteria to yield lactic and acetic acids. The consequent fall in intestinal pH suppresses ammonia production and reduces ammonia absorption.

Gut sterilisation. In human medicine neomycin is given orally to sterilise the bowel. Neomycin (20 mg/kg orally BID) has been found of little use in dogs in this respect and carries the potential disadvantage that it may alter the bacterial flora of the bowel and so interfere with the degradation of lactose.

Table 6.2: Classification of antibacterials according to the ease with which they may enter the brain

	Bactericidal	Bacteriostatic
Group A Reach adequate concentrations in the brain	potentiated sulphonamides; certain cephalosporins (eg. cefotaxime)	chloramphenicol
Group B Reach adequate concentrations only in presence of inflammation	penicillins	certain tetracyclines (e.g. doxycycline) and macrolides (e.g.erythromycin)
Group C Do not reach adequate concentrations even in presence of inflammation	aminoglycosides other cephalosporins	other tetracyclines other macrolides

An IV infusion of 5% dextrose may be used as a way of raising blood glucose and promoting conversion of ammonia to glutamate.

Thiazide diuretics should be avoided as they may cause an hypokalaemic alkalosis and hence promote renal synthesis of ammonia and ammonia absorption.

Infections of the Central Nervous System

Viral infections

No specific treatment is available for viral infections of the central nervous system such as canine distemper or feline infectious peritonitis. In cases where there is evidence of cerebral oedema, anti-oedema doses of dexamethasone (2.2 mg/kg) may be used but should not be repeated frequently on account of its side effects.

Bacterial meningoencephalitis

General principles. In the treatment of infections of the nervous system, as in bacterial infection in general, the choice of antibacterial agent is governed by two main criteria: that the agent chosen should be active against the organism(s) concerned and that it should attain effective concentrations over a period of time at the site of infection. The latter presents a particular problem in the case of the brain because of the blood-brain barrier, which limits access of drugs to the brain from the systemic circulation. In most body tissues drugs are able to diffuse from the blood into tissue fluid through gaps between the capillary endothelial cells. In the brain, however, the endothelial cells are joined by tight junctions so that drugs can enter the brain only by the transcellular route, that is only if they are sufficiently lipid-soluble to diffuse across the membranes of the endothelial cells. The blood-brain barrier may be bypassed by intrathecal injection, although this technique is rarely employed in veterinary medicine. When the meninges are inflamed, permeability to certain drugs is increased and on this basis antibiotics may be grouped into three classes as show in Table 6.2.

There is some debate as to whether drugs of Group B may be inferior to those in Group A because, as inflammation subsides, they may no longer be able to penetrate to clear the infection. Whichever antibacterial agent is used it may be beneficial to give the first dose by the intravenous route to ensure high initial tissue concentrations .

Bacteriostatic or bactericidal. The immune system of the brain is deficient relative to many other tissues and as a result a bactericidal agent is to be preferred for the treatment of brain infections. To this end the agents in Table 6.2 have also been classified as bacteriostatic or bactericidal.

Organisms involved. The organisms most commonly found in cases of bacterial meningoencephalitis in the dog and cat are streptococci, staphylococci, pasteurella and, occasionally, coliforms.

Agents of choice. In the absence of precise identification of the organisms concerned, ampicillin would appear to be the agent of choice. Alternative agents are: for staphylococci and streptococci - benzylpencillin or cefotaxime; for pasteurella - benzylpencillin or potentiated sulphonamides; for coliforms - potentiated sulphonamides or chloramphenicol.

Ancillary treatment. Bacterial meningoencephalitis is often accompanied by cerebral oedema and, to limit the extent of this, excessive fluid intake should be avoided. Corticosteroids reduce cerebral oedema and other inflammatory changes but in so doing impair host defences and, by reducing inflammation, retard entry of group B antibiotics into the brain. Controlled trials have failed to show any benefit of corticosteroids in bacterial meningitis. The same does not apply to brain abscesses. Trials in cats have shown that in this condition combined use of corticosteroids and antibiotics is superior to antibiotics alone. Bacterial meningoencephalitis in dogs is frequently accompanied by a marked fever which may be reduced by administration of acetylsalicylic acid (Aspirin).

Table 6.3: *Agents for the treatment of systemic mycoses*

Generic Name	Brand Name	Activity	Comments
amphotericin	Fungizone®	Fungi (eg. Aspergillus) and yeasts (eg. Cryptococcus, Candida)	IV only renal toxicity
ketoconazole	Nizoral®		oral, hepato-toxicity
flucytosine	Alcobon®	Yeasts only (eg. Cryptococcus, Candida)	oral

Mycotic infection

The most common mycotic infection of the CNS of dogs and cats is Cryptococcus. Table 6.3 lists the agents most commonly used for the treatment of systemic mycoses in domesticated animals.

Amphotericin acts by damaging the cell membrane and in so doing increases permeability to flucytosine so that the two are synergistic and the therapy of choice for systemic cryptococcosis is flucytosine (Alcobon®) 100-150 mg/kg/day orally in divided doses together with amphotericin (Fungizone®) 0.25-0.5 mg/kg IV three times weekly. Renal function should be monitored regularly to detect any renal damage caused by amphotericin. Unfortunately, while flucytosine enters the CNS, amphotericin does not and so the latter is not effective against intracranial organisms. Flucytosine must be given until remission occurs. Toxic hazards following long-term flucytosine administration include oral and cutaneous ulceration, enterocolitis and depressed bone marrow function.

The alternative treatment is ketoconazole (Nizoral®) 10 mg/kg daily orally, but this may cause liver damage.

Corticosteroids are positively contraindicated in mycotic infections which are most commonly seen in immuno-compromised animals, often following corticosteroid therapy.

Granulomatous Meningoencephalomyelitis (Primary Reticulosis)

Prednisolone 1 - 2 mg daily orally may bring about a temporary improvement in this condition but does not affect the long-term outcome.

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CHAPTER SEVEN

Seizures and Epilepsy

Richard A. LeCouteur

INTRODUCTION

Seizure disorders occur frequently in dogs and cats. Estimates of seizure incidence during a lifetime vary from 0.5% to 5.7% of all dogs, and from 0.5% to 1.0% of all cats (LeCouteur and Child 1989). Discussion of seizure disorders of all types must precede consideration of the clinical management of epilepsy. Such a broad approach is necessary because dogs and cats with a seizure disorder frequently have similar histories and physical signs despite a wide variety of underlying causes of cerebral dysfunction (including epilepsy). Similarities in clinical histories of dogs or cats with a seizure disorder reflect the similar pathophysiological mechanisms that underlie seizure disorders of all types (Wheeler 1990).

Definition of Terms

Seizures are the clinical manifestation of a paroxysmal cerebral disorder, and result from a transitory disturbance of brain function (Bunch 1986; LeCouteur and Child 1989; Schwartz-Porsche 1994). A seizure is paroxysmal because of its tendency to appear suddenly out of a background of normality and then disappear with equal abruptness (Holliday 1980a; Holliday 1980b). The terms *fit* and *ictus* are synonymous with the term *seizure* and refer to any type of paroxysm. A *convulsion* is any episode that includes a period of generalised clonic and tonic muscle activity accompanied by loss of consciousness (Holliday 1980a).

Epilepsy includes any of several non-progressive intracranial disorders that induce recurrent seizures of any type (Holliday 1980a; Holliday 1985). The seizures of epilepsy may be accompanied by characteristic electroencephalographic (EEG) events (Klemm 1989). This definition of epilepsy includes those disorders caused by genetically determined primary brain dysfunction (*inherited epilepsy*) and those brain disorders that, although previously active, have become inactive and have left the brain in a "seizure-prone" state (*acquired epilepsy*) (Holliday 1980b; Holliday 1985). Also included in this definition are a group of disorders that result from non-progressive intracranial brain dysfunction that has neither an inherited nor an acquired basis and for which the exact cause or mechanism for the seizures cannot be decided (*idiopathic epilepsy*) (Farnbach 1984). Excluded from this definition of epilepsy are genetically determined intracranial disorders that induce seizures as one manifestation of a spectrum of clinical signs and structural alterations. Also excluded, regardless of chronicity, are acquired disorders that induce seizures as part of a progressive brain-destructive process (Holliday 1985).

Epilepsy has been defined by several authors as "any condition in which seizures recur" (Fenner 1986; Oliver 1987; Russo 1988). This broad definition includes many progressive brain disorders, such as cerebral neoplasia, which may require definitive treatment in addition to control of seizures by means of anticonvulsant medications. The term *"symptomatic epilepsy"* has been used to describe seizures resulting from such progressive intracranial causes, and the term *"true epilepsy"* has been used to describe seizures resulting from non-progressive intracranial causes. This approach may be confusing, as it is difficult for some animal owners to make the distinction between "true" and "symptomatic" epilepsy, yet the distinction is essential for accurate diagnosis and therapy of a seizure disorder. A logical approach to the diagnosis and treatment of epilepsy requires that both extracranial causes and progressive intracranial causes of seizures are excluded before a diagnosis of epilepsy is made. Restriction of the term epilepsy to include only *non-progressive intracranial disorders that induce recurrent seizures* helps ensure accurate diagnosis of disorders other than epilepsy that may cause seizures. This in turn ensures the institution of appropriate therapy for disorders other than epilepsy that may require specific treatment in place of, or in addition to, anticonvulsant medication (LeCouteur and Child 1989).

Classification of Seizures

An epileptic seizure is a definable event that may be measured, recorded, and classified. Classification of epileptic seizures is well-established in people (Table 7.1) (Schwartz-Porsche 1994). Therapy for epilepsy of people is best directed toward the seizure type. A description of seizures learned from a history (or

Table 7.1: International classification of epileptic seizures in people

I. **Partial Seizures** (local,focal)
- A. Simple partial seizures (consciousness not impaired)
  1. With motor symptoms
  2. With somatosensory or special-sensory symptoms
  3. With autonomic symptoms
  4. With psychic symptoms
- B. Complex partial seizures (consciousness impaired)
  1. Beginning as a simple partial seizure and progressing to impairment of consciousness
  2. With impairment of consciousness at onset
- C. Partial seizures evolving to secondary generalised seizures

II. **Primary Generalised Seizures** (bilaterally symmetrical without local onset; consciousness may be impaired or lost)
- A. Absence seizures
- B. Myoclonic seizures
- C. Clonic seizures
- D. Tonic seizures
- E. Tonic-clonic seizures
- F. Atonic seizures

III. **Unclassified Epileptic Seizures** (inadequate or incomplete data)

From Commission on Classification and Terminology of the International League Against Epilepsy: Proposal for revised clinical and electroencephalographic classification of epileptic seizures (1981). *Epilepsia* **22**, 489.

occasionally by means of videotape) is the single most important factor in providing a correct therapeutic approach in people.

A classification system specifically for cats and dogs does not exist. Many types of epileptic seizure that occur in animals, however, are similar to those described for people, and attempts have been made to classify epileptic seizures of cats and dogs by using a system of classification designed for people. A classification system that is designed specifically for dogs and cats is needed to permit understanding and comparison of prospective studies of anticonvulsant efficacy in animals (Parent 1988). The initial step in the classification of epileptic seizures of dogs and cats is to categorise the seizures as either partial *(focal)* or *generalised* episodes (Schwartz-Porsche 1994).

Partial seizures

Partial seizures are those in which a localised onset may be determined. Such a determination may be based on many factors. This differs from the classification in people, however, where the nature of the clinical seizure and the character of the EEG are the major criteria. Partial seizures usually have a congenital or an acquired cause (such as neoplasia or encephalitis) (Holliday 1980b). In animals attempts have been made to subdivide partial seizures into simple and complex partial seizures (Schwartz-Porsche 1994). Either partial seizure type may evolve into a secondary generalised seizure.

Simple partial seizures occur without impairment of consciousness, and may emerge as focal motor, sensory, somatosensory, autonomic, and/or psychic phenomena (Schwartz-Porsche 1994). They occur infrequently in cats and dogs, and should they occur, motor signs usually predominate (twitching of individual muscle groups, tonus or clonus of an extremity, or turning of the head).

Complex partial seizures are accompanied by impairment of consciousness, and are sometimes referred to as psychomotor seizures (Schwartz-Porsche 1994). Recognition of this type of seizure poses problems, as impairment of consciousness is often difficult to recognise in cats or dogs. Animals affected by complex partial seizures may appear confused and restless, pupils may be dilated, and occasionally there is slight twitching of facial muscles. Behavioural disturbances are frequently seen, consisting of barking or howling, involuntary activity such as licking or chewing, and even aggressive or defensive behaviour. Aggressive behaviour frequently occurs during complex partial

seizures of cats. An episode of complex partial seizures of cats may persist for several hours.

Primary generalised seizures

Generalised seizures are the most frequently recognised seizures in dogs and cats (Schwartz-Porsche 1984; Frey 1986). Evidence of localised onset does not appear in the clinical manifestations of the seizure or in EEG findings (Schwartz-Porsche 1994). The most frequently recognised generalised seizure type in animals is the *generalised tonic-clonic (grand mal) seizure*, however other seizure types have been described, including *absence seizures* and *myoclonic seizures*.

Absence seizures (or petit mal) of people are characterised by a sudden brief loss of consciousness, and typical EEG events, that may be accompanied by mild motor and/or vegetative events (Schwartz-Porsche 1994). These seizures have not been reliably confirmed to occur in cats or dogs, however events that appear similar to the description of absence seizures in people have been noted.

Myoclonic seizures are characterised by a sudden brief contraction ("muscle jerk") of one or more muscles (Schwartz-Porsche 1994). The muscle contractions may occur in rapid succession, and secondary generalisation may follow. Myoclonic seizures have been recognised in association with Lafora's disease (myoclonic epilepsy), a storage disease that may occur in ageing Basset hounds (Kaiser *et al* 1991).

Clonic seizures consist of rhythmic muscle contractions that resemble generalised seizures, but lack a tonic component. These seizures may occur more frequently in cats than in dogs, and may be difficult to distinguish from complex partial seizures (Schwartz-Porsche 1994).

Tonic seizures are seen primarily in dogs (Poodles, Dachshunds, Terriers), may occur with or without loss of consciousness, and consist of an increase in muscle tone in all skeletal muscles (Schwartz-Porsche 1994). Tonic seizures may last from minutes to several hours.

Tonic-clonic seizures - Generalised tonic-clonic seizures represent about 60% of all epileptic seizures seen in cats, and about 80% of those seen in dogs (Schwartz-Porsche 1994). They usually are accompanied by loss of consciousness, and consist of a tonic phase, during which increased muscle tone causes the animal to fall to its side, and a clonic phase, consisting of intense muscle jerking.

The sequence of events that make up a generalised tonic-clonic seizure vary considerably between animals, but always follow a similar basic pattern. The sequence may be divided into three stages: *the prodromal stage, the ictus,* and *the postictal stage*. Some authors refer to part of the prodromal stage as the "aura", however this term refers to the focal onset of seizures consciously experienced by people, and as such, cannot truly be appreciated in animals that are unable to verbally communicate the phenomenon.

The *prodromal stage* varies greatly in duration and intensity, and may not be evident in all animals that experience a generalised seizure. This stage may last from minutes to days before the ictus begins. The prodromal stage may consist only of a slight alteration in behaviour, or may involve a period of restlessness where the animal may run around, vocalise, seek refuge, salivate, or vomit.

The *ictus* (actual seizure) begins either suddenly or focally. Should the onset be sudden, which is the case in idiopathic epilepsy, the tone of all skeletal muscles increases suddenly and the animal loses consciousness. Symmetrical orofacial movements may precede the tonic phase. The jaws may be either wide open or clenched closed, and pupils are dilated and fixed. Clonic movements often are superimposed on or begin during the tonic phase, and become predominant as the tonic phase wanes. Violent jaw movements, excessive salivation, involuntary urination, and defecation, may occur during this stage. Following the clonic phase, walking or running movements occur. The ictus lasts from a few seconds up to several minutes.

In the *postictal stage* some cats may remain motionless for prolonged periods, whereas dogs either fall into a deep sleep, or remain lying down. Most animals stand up after a few seconds or minutes. At first they are disorientated, wander around restlessly, are unresponsive, and may appear blind and deaf. As their state normalises, they often become extremely hungry and/or thirsty. This postictal behaviour lasts from a few seconds to hours or even days.

Causes of Seizures

The normal brain is capable of convulsing in response to a variety of stimuli within the central nervous system and to many external influences. Consequently, the causes of seizures are numerous (LeCouteur and Child 1989; Schwartz-Porsche 1994). Disorders that induce seizures may arise either outside the nervous system (*extracranial causes*) or within the nervous system (*intracranial causes*) (Table 7.2). Each of these groups of causes may be divided in turn into two categories (Holliday 1980b). Extracranial causes are divided into those that originate outside the body (e.g. toxic agents) and those that arise within the body but outside the nervous system (e.g. hypoglycaemia). Intracranial causes of seizure disorders may be divided into progressive and non-progressive diseases. Progressive causes of seizure disorders include those diseases that, in time, may affect an increasing volume of brain tissue (e.g. neoplasia), and may produce clinical signs other than seizures. Non-progressive intracranial causes of

Table 7.2: Causes of seizure in dogs and cats

Extracranial causes		Intracranial causes	
Originate outside body (e.g., toxic diseases)	Originate inside body (e.g., metabolic diseases)	Progressive* (e.g., neoplastic or infectious)	Non-progressive* (epilepsy)

* Note that the terms "progressive" and "nonprogressive" refer to the cause of the seizures. The seizures may progress in frequency or severity with time, however the cause of the seizures may not progress.

seizures include inherited, acquired, and idiopathic epilepsy.

Clinically, it is essential to distinguish between progressive and non-progressive brain diseases that produce seizures. Therapy for progressive diseases requires not only control of seizures but also specific therapy for the underlying disease. If therapy of the underlying disease is not possible, the veterinarian should at least provide an accurate diagnosis and prognosis. On the other hand, it is seldom possible to make a precise aetiological or anatomical diagnosis in non-progressive seizure disorders of intracranial origin (i.e. epilepsy). Once the non-progressive nature of the cause of a seizure disorder is established, therapy with an anticonvulsant medication is indicated.

Extracranial disorders

Extracranial disorders may alter brain metabolism and electrophysiology, leading to paroxysmal discharges and seizures. Because the disorders affect both hemispheres, primary generalised seizures usually occur, although other clinical signs may be superimposed on them. Extracranial disorders frequently result from various metabolic conditions, such as hypoglycaemia, liver disease, hyperlipoproteinaemia, renal disease, hypocalcaemia, and hypothyroidism. Toxicoses, including lead or organophosphate poisoning, caffeine or theobromine toxicosis (from excessive chocolate consumption) may also result in seizures. Intestinal parasitism and hyperthermia are other extracranial causes of seizures.

Intracranial disorders

Intracranial causes of seizures include malformations (e.g. hydrocephalus), inflammatory disorders (e.g. canine distemper encephalitis), nutritional disorders (e.g. thiamine deficiency), neoplasia, cranial trauma, degenerative conditions (e.g. storage diseases), and cerebral infarction (Schwartz-Porsche 1994). Affected animals typically present with progressive neurological disease. In some animals, such as animals with a previous history of cranial trauma, morphological brain lesions may have occurred long before the first seizures occur, and may be inactive but leave the brain in a seizure-prone state. In other animals, seizures may be an early sign of progressive brain disease, such as cerebral neoplasia, and may be the sole clinical sign for a prolonged period.

With intracranial disease, secondary or primary generalised seizures occur in a wide variety of clinical manifestations, depending on the location and extent of the underlying lesion(s). The frequency of seizures may vary considerably, and the association with rest and sleep seems to be less pronounced than in idiopathic epilepsy (see later). Most intracranial diseases lead to other neurological or clinical signs during the interictal period, and these diseases may have a progressive or non-progressive clinical course.

Epilepsy

The seizures seen in association with idiopathic epilepsy are caused by functional disorders of the brain in which both hemispheres are affected by paroxysmal neuronal discharges (Schwartz-Porsche 1994). Epileptic seizures are generalised and symmetrical from the onset (Schwartz-Porsche 1994). Morphological lesions are not observed in the cerebrum of animals with epilepsy, with the exception of animals with microdysgenesis (a condition where subtle alterations of embryo-foetal development, such as increased neuron density, may result in a lowered seizure threshold) (Schwartz-Porsche 1994). However, lesions such as gliosis, atrophy, or laminar cortical necrosis, may occur secondary to severe seizures, clusters of seizures, or status epilepticus (Yamasaki *et al* 1991). These lesions may evolve into a secondary epileptic focus (Schwartz-Porsche 1994).

Idiopathic epilepsy of dogs or cats usually begins with a single seizure (Schwartz-Porsche 1994). The seizures most often occur during or following a period of sleep or rest, and rarely occur during periods of activity. Seizure frequency is variable (days to months between seizures), however the time between seizures usually decreases as the disorder becomes more chronic.

Intervals between seizures may be uniform, or highly variable. Clusters of seizures may occur over hours or days in some breeds of dog (e.g. German shepherd dogs, Saint Bernard dogs, Irish setters).

Diagnostic Approach to a Seizure Disorder

A comprehensive case history, complete physical and neurological examinations, and a minimum data base consisting of results of haematological and serum chemistry analyses should be obtained for all animals suspected of having a seizure disorder, even if only one seizure has been observed. On the basis of this information a list of differential diagnoses should be made. Further clinical laboratory, toxicological, or radiographic procedures may be indicated after the results of these initial tests are known (Table 7.3).

History

The environment, nutritional status, immunisations, birth complications, previous illnesses or injuries, age at onset of seizures, type and frequency of seizures, possible occurrence of localising signs before or during the ictus, and interictal signs, may provide important diagnostic information. Of particular interest are a *description of the seizures* and the *age, breed and gender* of the animal.

Description of seizures - A description of an animal's seizures, their frequency and duration, and the animal's behaviour between seizures (interictal period) may be helpful in determining the cause of a seizure disorder. It is very useful if the owner can obtain a videotape of the episode.

It is important to determine whether a seizure has occurred and to distinguish it from a syncopal episode (resulting from cardiac and / or pulmonary disease), narcolepsy or cataplexy, or episodic weakness (resulting from myasthenia gravis, polymyopathy, polyneuropathy or metabolic abnormality). Any involuntary phenomenon that is episodic and recurrent should be evaluated as a seizure. Tonic and clonic muscle movements, with or without loss of consciousness, accompanied by signs of autonomic disturbance such as urination, defecation, or salivation are highly suggestive of a seizure. Loss of consciousness accompanied by muscle flaccidity is more often associated with narcolepsy or syncopal episodes. Collapse and muscle flaccidity without loss of consciousness are more consistent with episodic weakness resulting from a motor unit disease or metabolic dysfunction.

Partial seizures are characterised by a localising sign that is indicative of the part of the brain acting as the epileptogenic focus (Holliday 1980a). The localising sign may be motor, sensory, or behavioural in nature, depending on the area of the brain affected. Animals may turn their head to one side, show tonus and / or clonus in one limb or ipsilateral thoracic and pelvic limbs, or adopt abnormal postures. Sensory disturbances probably occur in animals but rarely are recognised. Animals may or may not appear to lose consciousness. If seizures originate from portions of the limbic system, they may appear as behavioural changes. These seizures have been termed psychomotor seizures and may be referred to as partial seizures with complex symptomatology. The clinical signs include somnolence, aggression, appetite changes, aimless running, screaming or barking, attacking inanimate objects, and chewing or licking movements. Autonomic signs (salivation, urination) may predominate. Behavioural disorders such as fly biting, tail chasing, or flank sucking may reflect partial seizure activity. A partial seizure may progress to a generalised seizure within seconds or minutes and localising signs may be present only briefly before the onset of a tonic-clonic seizure. Jacksonian seizures, which are characterised by a slowly spreading tonic spasm in one limb that may extend along one side of the body and then to the other side, rarely occur in dogs and cats. These seizures arise from the sensorimotor cortex in carnivores.

Seizures that are generalised from the time of onset appear to be synchronous and symmetrical throughout the entire body. Clinical signs include loss of consciousness, a tonic phase characterised by extension of the limbs, opisthotonus, and apnea that may last several seconds to several minutes followed by a clonic phase characterised by alternating contraction and relaxation of muscles of similar duration. The clonic phase is followed by a period of walking or running (paddling) movements. Urination, defecation, and / or salivation commonly occur during a seizure. Chewing movements of lips, jaws, and tongue may occur during a generalised seizure and may be seen at the onset of a seizure. Many animals do not exhibit preictal signs, but some owners report a change in an animal's behaviour or expression. In addition, some animals search for their owners, hide from them, or cry out before the onset of a seizure. After the animal has regained consciousness it may appear normal immediately or may be depressed, confused, appear blind, bump into objects, or in some cases become aggressive for minutes to several hours after a seizure. This postictal phase may be longer (hours or days) in animals that have had multiple seizures in a short period of time.

The type of seizure seen in dogs or cats may be useful in determining the nature of the underlying cause. Generalised seizures are characteristic of most metabolic and toxic causes of seizures, and of inherited or idiopathic epilepsy. Partial seizures usually are seen in animals with an acquired focal or multifocal cerebral abnormality that may be progressive or non-progressive (e.g. congenital cerebral abnormalities, neoplasia, encephalitis, or a previous episode of cerebral hypoxia, ischaemia, trauma, or infection). However, partial seizures may be seen in animals with a metabolic encephalopathy that would be expected to

Table 7.3: Diagnostic approach for a seizure disorder in dogs or cats

HISTORY
(Description of seizures, age, breed, sex, etc.)

PHYSICAL AND NEUROLOGICAL EXAMINATIONS

MINIMUM DATA BASE
a. Complete blood count
b. Serum chemistry profile
c. Urinalysis
d. Fasting blood glucose level
e. Serum lead level*
f. Faecal parasite or ova examination*
g. Thoracic and/or abdominal radiographs*

ABNORMAL RESULTS
(Extracranial cause likely)

CONSIDER ADDITIONAL DIAGNOSTIC TESTS**
a. Pre-and postprandial bile acid determination
b. Serum insulin level, amended serum insulin:serum glucose level
c. Serum titres for CDV infection, FIP, toxoplasmosis, mycoses, etc.
d. Serum testing for FIV, FeLV, etc.
e. ACTH stimulation test
f. TSH stimulation test
g. Biopsy of extracranial neoplasm
h. Other tests as indicated

ABNORMAL RESULTS
(Extracranial cause confirmed)

Institute Specific Therapy for Cause of Seizures ± Anticonvulsant Therapy

NORMAL RESULTS
(Or continuation/worsening of seizures despite appropriate therapy for extracranial cause)

NORMAL RESULTS
(Intracranial cause likely)

CONSIDER ADDITIONAL DIAGNOSTIC TESTS**
a. CSF analysis
b. Skull radiographs
c. CT or MRI images of head
d. Electroencephalography+
e. Other tests as indicated

ABNORMAL RESULTS
(Intracranial progressive cause likely)

Consider Additional Diagnostic Tests**
a. CSF culture (bacterial, mycotic)
b. Serum and/or CSF titres for CDV infection, FIP, toxoplasmosis, mycoses, etc
c. Serum testing for FeLV,FIV, etc
d. Brain biopsy
e. Other tests as indicated

NORMAL RESULTS
(Intracranial nonprogressive cause likely)

EPILEPSY
a.idiopathic
b.inherited
c.acquired

Anticonvulsant Therapy

*Optional tests-completion depends on results of physical and neurological examinations, age of affected animal, etc.
**Decision to perform additional tests and selection of appropriate tests based on results of previously completed diagnostic tests, age of the animal, results of physical and neurological examinations, frequency of seizures, and response to previous anticonvulsant therapy.
+Electroencephalography is most helpful in the diagnosis of congenital brain malformations (eg, hydrocephalus, lissencephaly), and should not be considered a definitive diagnostic procedure for most other brain disorders of dogs or cats, including epilepsy.
CDV = canine distemper virus; FIP = feline infectious peritonitis; FIV = feline immunodeficiency virus; FeLV = feline leukaemia virus; ACTH = adrenocorticotrophic hormone; TSH = thyrotropin stimulating hormone; CSF = cerebrospinal fluid; CT = computed tomography; MRI = magnetic resonance imaging.

cause generalised seizures, and partial seizures with or without secondary generalisation may be seen in animals with inherited epilepsy (e.g. Beagle and Horak's laboratory dogs) and also in animals with idiopathic epilepsy that do not have pathological evidence of concurrent or prior intracranial disease. Psychomotor seizures may be seen in animals with lead poisoning. Similarly, animals with focal intracranial disease such as neoplasia may exhibit generalised seizures without localising signs.

The frequency and duration of seizures also are of importance in determining further diagnostic procedures that may be necessary and in deciding therapy. An increase in the frequency of seizures, especially in older animals, may be an indication of a progressive intracranial disease such as neoplasia, and investigation of possible intracranial causes of seizures is then warranted. It is important to determine if seizures occur at a certain time of the day or if they are related to exercise or feeding. Certain metabolic encephalopathies such as hypoglycaemia or hepatic encephalopathy result in seizures at times related to feeding. The frequency of seizures in animals may be difficult to establish, and an owner should be questioned about both known seizure episodes and any suspected seizures (e.g. evidence of urination and / or defecation in inappropriate places or abnormal behaviour such as that seen in the postictal phase of a seizure).

Owners often overestimate the duration of an animal's seizure. Usually seizures last from several seconds to minutes. If an animal has seizures that last longer than several minutes or seizures that occur in "clusters" (in which more than one seizure occurs within a 24-hour period) or episodes of status epilepticus (in which an animal has repeated seizures without regaining consciousness), anticonvulsant therapy usually is indicated regardless of the frequency of the seizure episodes.

Age, breed and gender - The cause of seizures often is related to the age of an animal. Therefore, the age of onset of seizures is important in forming a diagnostic plan for an animal with a history of recurrent seizures. Generally, animals with idiopathic epilepsy or a suspected inherited predisposition to seizures have their first seizure between six months and five years of age, although seizures may not be recognised until an animal is older than five years of age (LeCouteur and Child 1989). In some cases, however, epilepsy may be recognised in dogs younger than six months of age. Seizures may occur at an earlier age in offspring of epileptic dogs, and with increased inbreeding (Schwartz-Porsche 1994). Acquired epilepsy may result in onset of seizures at any age, and seizures may not occur for as long as four years after the initial cerebral insult that resulted in development of a seizure focus.

Epilepsy inheritance has been proven in Beagles (Biefelt *et al* 1971) and Horak's laboratory dogs (Holliday 1980b). Data suggest epilepsy may be genetically determined in breeds such as Belgian (Tervuren) shepherd dogs, German shepherd dogs (Britain), Keeshonds, and Collie dogs (LeCouteur and Child 1989; Schwartz-Porsche 1994). Several breeds of dogs have been reported to have a high incidence of idiopathic epilepsy. These include Golden retriever dogs, Irish setters, Saint Bernard dogs, German shepherd dogs, American cocker spaniels, Wire-haired fox terriers, Alaskan malamutes, Siberian huskies, and Miniature poodles (Schwartz-Porsche 1994). Epilepsy may have an inherited basis in these breeds, although genetic studies have not been performed. Idiopathic epilepsy may occur in dogs of any breed, including mixed-breed dogs. In one study, the incidence of seizure disorders appeared to be constant across breeds and mixed-breed boundaries (Farnbach 1984). In the same report, the high frequency of seizure disorders in certain breeds was shown to reflect the popularity of these breeds. Idiopathic epilepsy also occurs in cats and may be the cause of seizures in as many as 28% of cats with seizures (Lane and Bunch 1990). Acquired epilepsy may occur in any breed of dog or cat.

Seizure disorders in dogs and cats generally do not appear to have a sex predilection. Nevertheless, inherited epilepsy in Beagles more frequently affects males than females (5:1) (Biefelt *et al* 1971). A higher incidence of epilepsy also has been reported in male German shepherd dogs in Britain (Falco *et al* 1974) and Keeshonds (Wallace 1975). An increased frequency or severity of seizures may be seen in female dogs during oestrus or pregnancy (Shell 1984).

Miscellaneous considerations - Other factors are important in determining the possible causes of seizures. For example, does the animal have a known history of head trauma (especially if accompanied by loss of consciousness), meningitis, encephalitis, systemic infection, hypoxic episode or difficult birth, toxin exposure, or access to possible toxins such as lead-containing paint or linoleum in old houses? Is there a history of seizures in a related animal? Has the animal been vaccinated for canine distemper and is the vaccination current? What is the animal's diet?

Physical examination

A thorough physical examination is important in all animals with a seizure disorder. Cardiac or respiratory abnormalities may result in syncope or episodic weakness, which the owners may interpret as seizures. Tumours outside the calvaria may have metastasised to the skull, meninges or brain, resulting in seizures. Nasal discharge or epistaxis may be associated with nasal tumour or infection that may also extend intracranially. Systemic illness or endocrine abnormalities also may result in seizures. Palpation of the skull may

detect abnormalities associated with trauma, tumours, or congenital defects.

Ophthalmoscopic examination may detect chorioretinitis associated with viral, fungal, or protozoal CNS infection. Papilloedema resulting from increased intracranial pressure may be present in animals with congenital or acquired hydrocephalus, neoplasia, or CNS infection.

Neurological examination

A thorough neurological examination is also important in animals with a history of seizures. Animals with epilepsy usually are neurologically normal between seizures, whereas animals with seizure disorders as a result of toxic, metabolic, congenital, neoplastic, or inflammatory disease often have neurological abnormalities between seizures. However, animals with acquired epilepsy may have other neurological deficits in addition to seizures, and seizures may be the only abnormality in some animals with CNS neoplasia or metabolic abnormalities such as hypoglycaemia or lead poisoning.

When possible, it is important to examine animals between seizures and when the animal is not in a postictal state. Many animals show temporary neurological abnormalities (blindness, weakness, behaviour change) for minutes to hours after a seizure. Animals that have had an episode of status epilepticus or a cluster of seizures may require several days to one week without further seizures before a reliable neurological examination may be performed. Neurological examination findings may also be affected by CNS depressant drugs such as anticonvulsant or anaesthetic agents.

Minimum data base

A complete blood count, serum chemistry profile, including a fasting blood glucose, calcium, BUN, albumin, total protein, cholesterol, triglycerides, ALT, and alkaline phosphatase determinations, and urinalysis should all be done for animals that have had one or more seizures to detect any metabolic or toxic cause of the seizure disorder or evidence of systemic infection. Blood samples should be collected after at least a 12-hour fast, because lipaemia seen after feeding may invalidate some results but, if present after fasting, lipaemia may be abnormal. Hypoglycaemia resulting from anorexia, illness, or metabolic dysfunction frequently causes seizures in dogs younger than six months of age. In older dogs (usually more than five years of age) hypoglycaemia may result from the presence of an insulin-secreting tumour (insulinoma). In these animals, fasting for more than 24 hours may be necessary to induce hypoglycaemia. Blood lead quantification should be done in an animal with possible exposure to lead-containing materials, in all animals from areas where the incidence of lead poisoning is high (big cities, areas with old houses, etc.) and in animals that are less than one year of age (as these animals have a higher incidence of lead poisoning). Blood lead quantification is the most reliable way of detecting lead poisoning, because haematological abnormalities are not always present and affected animals may or may not show abnormal behaviour between seizures.

Radiographs of the thorax or abdomen may be indicated as part of the minimum data base, particularly in animals older than five years of age or in animals in which results of a physical examination suggest abnormal pulmonary or cardiac function.

Faecal examination should be done in puppies with a seizure disorder. A heavy intestinal parasite burden may be associated with seizures, probably as a result of induced metabolic abnormalities such as anaemia or hypoproteinaemia. However the specific cause of seizures in these cases is usually undetermined.

Differential Diagnosis

Information obtained from the history, physical, and neurological examinations and the results of a minimum data base may be used to form a list of differential diagnoses. Idiopathic epilepsy may occur at any age, but it occurs most frequently in dogs or cats between six months and five years of age. Using idiopathic epilepsy as a reference point, a list of differential diagnoses for seizure disorders may be formed for each of three age groups: less than six months of age, six months to five years of age, and older than five years of age (Parent 1988). A list of the most common diseases other than epilepsy that may occur in association with seizures in each of these age categories is included in Table 7.4.

Additional Diagnostic Tests

Selection of additional tests should be based on results of physical and neurological examinations and on the results of tests that comprise a minimum data base (Table 7.3). The dog's or cat's age should also be considered because certain disorders that may result in seizures are more frequently associated with younger dogs and cats (Table 7.4) (Parent 1988).

An extracranial cause of seizures is most likely associated with an abnormal minimum data base (Table 7.3). Additional tests may be selected to investigate such extracranial causes. For example, in animals with serum chemistry abnormalities that are consistent with liver disease (e.g. low BUN, elevated ALT and / or alkaline phosphatase, low glucose, low total protein, etc.) further tests may be needed to assess liver function. Quantification of serum bile acids after a 12-hour fast, and 2 hours postprandially, provides a reliable indicator of liver function.

After confirmation of an extracranial cause for seizures, specific therapy may be indicated. In certain instances, anticonvulsant medication may be instituted in addition to specific therapy of an extracranial

Table 7.4: Most frequently occurring causes of seizures in dogs and cats other than epilepsy

Category of Disease	Less than 6 Months of Age	6 Months to 5 Years of Age	Greater than 5 Years of Age
Degenerative/ vascular	Storage diseases	Intracranial infarction, haemorrhage	Intracranial infarction, haemorrhage
Anomalous	Hydrocephalus Lissencephaly	Hydrocephalus Lissencephaly	
Metabolic	Hepatic encephalopathy (portocaval shunt) Hypoglycaemia	Hepatic encephalopathy Hypoglycaemia Hypocalcinaemia Hyperlipoproteinaemia Hyperkalaemia Uraemia Hypothyroidism etc.	Hepatic encephalopathy Hypoglycaemia Hypocalcaemia Hyperlipoproteinaemia Hyperkalaemia Uraemia Hypothyroidism etc.
Neoplastic		Primary brain Metastatic Local invasion	Primary brain Metastatic Local invasion
Infectious/ inflammatory	Viral: canine distemper, rabies, feline infectious peritonitis, etc. Bacterial: aerobic, anaerobic, abscess Mycotic: cryptococcosis, etc. Protozoal: toxoplasmosis, etc. Rickettsial: Ehrlichiosis, etc.		
Parasitic	Fleas, hookworms		
Idiopathic	Granulomatous meningoencephalomyelitis Pug dog encephalitis		
Traumatic	Cranial trauma Cerebral hypoxia / anoxia		
Toxic	Lead Organophosphate Strychnine, etc.		

disorder to control seizure activity during such therapy. Depending on the nature of the underlying extracranial disease, such anticonvulsant therapy may or may not be discontinued at some later date.

It should be remembered that in rare instances both an extracranial and an intracranial disorder may be present, and yet the extracranial disorder may not be related to the cause of the seizures. For example, it is possible that a dog with seizures may have hepatic cirrhosis and a primary intracranial neoplasm. For this reason, it is essential to monitor closely the response of an animal to therapy for an extracranial cause of seizures. Should the seizures continue or worsen in the face of a response to therapy of the extracranial disease, then further diagnostic tests may be indicated.

An intracranial cause of seizures is most likely associated with normal results of a minimum data base (Table 7.3). An intracranial cause should also be considered if the results of additional tests completed to fully investigate abnormalities seen on a minimum data base prove to be normal. Cerebrospinal fluid (CSF) analysis is essential for any dog or cat in which an intracranial cause for seizures is suspected. In addition to submission of CSF for cytological examination and protein quantification, aerobic and anaerobic bacterial and / or mycotic culture and sensitivity testing may be done, and titres for infectious agents may be completed (e.g. cryptococcosis, canine distemper, etc.). Radiographs of the skull may be useful for detecting calvarial tumours, mineralised intracranial neoplasms, or fractures of the skull associated with head trauma.

Electroencephalography (EEG) is helpful in the diagnosis of congenital malformations such as hydrocephalus or lissencephaly. The EEG can also be useful to evaluate electrical events associated with a seizure that may occur during recording and in the identification of paroxysmal electrical events that occasionally occur interictally in the recordings of some epileptic animals (Klemm 1989). Advanced imaging modalities, such as X-ray computed tomography or magnetic resonance imaging, may provide specific information

regarding the location and extent of intracranial lesions such as neoplasms, granulomas, infarcts, or haemorrhages.

Animals more than six months and less than five years of age that have a history of a seizure or of recurrent seizures, that have normal physical and neurological examinations, and that have normal results on a minimum data base probably have a non-progressive intracranial disorder. Ideally, additional diagnostic procedures should be done in such animals, however, consideration of costs involved and potential for morbidity and mortality associated with anaesthesia may result in a decision to delay further tests pending assessment of response to anticonvulsant medication. If a response to therapy is not seen, if seizure frequency or severity increase, or if additional clinical signs develop, then further diagnostic tests to investigate progressive intracranial causes of seizures should be done.

Anticonvulsant Therapy

Therapy for a seizure disorder depends on accurate determination of the cause of the seizures. Treatment with anticonvulsants is indicated for animals with idiopathic epilepsy. Seizures resulting from a structural brain disorder (progressive intracranial disease) require additional therapy, depending on the cause of the disease (e.g. neoplasia or inflammation). Anticonvulsants usually are contraindicated in animals with extracranial causes of seizures, where therapy should be directed towards the primary cause of the seizures (e.g. hypoglycaemia).

Objectives of anticonvulsant therapy

While the overall goal of anticonvulsant therapy is to eradicate all seizure activity, this goal is rarely achieved (Bunch 1986). Most dogs and cats benefit from anticonvulsant medication by *reduction in frequency, severity, and duration of their seizures* (Parent 1988). A realistic goal is to reduce seizure frequency to a point that is acceptable to an owner without intolerable or life-threatening adverse affects to the animal.

General principles of anticonvulsant therapy

Prevention of seizures in cats or dogs with epilepsy is a pharmacological problem in clinical veterinary medicine (Holliday 1980b). Surgical therapy for uncontrolled epilepsy as applied in humans has not yet been reported for use in animals.

Prior to initiation of therapy for seizures induced by epilepsy, every reasonable effort must be made to rule out either extracranial or progressive intracranial causes for the seizures.

Decisions regarding the need for anticonvulsant therapy

Many factors must be considered prior to the initiation of anticonvulsant therapy. The most important considerations are *seizure frequency*, *seizure character*, and *owner factors*.

Seizure frequency - The seizures observed in epileptic animals occur with varying frequency, and two general approaches exist regarding the institution of anticonvulsant therapy. Some authors state that therapy should not be started before the recurrent nature of the disease has been established (Bunch 1986; Frey 1986). This means that at least two seizures should have been observed. Otherwise animals may be treated that would not have had additional seizures. However, there may be sound biological reasons for beginning treatment after the first seizure. Experience in human epilepsy indicates that when this is done, seizure control may be more effective (Parent 1988).

Character of seizures - In certain instances, early and aggressive control of seizures is required. For example, in those animals where preictal and postictal phases are characterised by intolerable changes in personality (e.g. aggression) or in excretory behaviour (Bunch 1986).

Owner factors - In veterinary practice, the decision for or against anticonvulsant therapy ultimately must be made by the owner of an epileptic dog or cat. This decision should be based on information and advice provided by a veterinarian. An owner should be fully informed about the nature of the disease and its treatment in terms that are easily understandable. The owner should have a realistic knowledge of the objectives of anticonvulsant therapy because frequently an owner will expect successful therapy to be curative with complete elimination of seizures. An owner must appreciate the need for regular administration of an anticonvulsant drug and also understand that an animal may require medication for the remainder of its life. Cost of medication and regular assessments by a veterinarian should be discussed. Alterations in dosage without prior consultation must not occur. Omission of a single dose may result in severe relapses and sometimes status epilepticus. Although seizure frequency and severity will be reduced in the majority of cats or dogs that receive anticonvulsant medications, a proportion of animals (perhaps as high as 20-30%) may not be controlled adequately despite intensive medical management. With high dosages of anticonvulsant medications, the risk of drug-induced complications increases and must be weighed against the benefits of therapy. Once therapy has begun, a prescribed dosage schedule must be followed exactly. An owner should have a detailed knowledge of expected undesirable effects of anticonvulsant medications. Knowledge of these factors is essential for a high and intelligent degree of cooperation between an owner and veterinarian. Euthanasia of an animal should be considered when an

owner cannot commit to supervision and lifetime treatment of a dog or cat with severe epilepsy.

General recommendations for anticonvulsant therapy

In general, owners should be encouraged to begin anticonvulsant medication in epileptic dogs or cats that are known to have had one or more seizures within an eight week period. Treatment is not routinely advised in animals with seizures that occur less frequently than once every eight weeks, as owners of such animals often do not follow instructions diligently and may treat animals only intermittently. Certain owners, however, are so distressed by seizures that occur in their pet that they are willing to medicate an animal daily despite a history of infrequent seizures.

In animals that have had only one seizure, institution of therapy may be delayed. Such a delay may permit the seizure interval to become apparent, thereby providing a basis for a decision regarding the need for therapy and also for an assessment of the efficacy of therapy once it is initiated.

Exceptions to these recommendations are made for animals that have seizures in clusters or episodes of status epilepticus even though the interval between clusters may be greater than eight weeks. The seizure episodes have a tendency to become more frequent and severe in such animals when control is not attempted.

When seizures have not occurred in a dog or cat for a period of 6-12 months, a cautious reduction of dosage may be attempted (Frey 1986). Such a reduction must be done slowly. However, it is rare for a dog or cat to remain free of seizures after withdrawal of drug therapy.

There are few alternatives to the use of pharmacological agents in the control of seizures. Acupuncture, either as a sole therapy or in conjunction with conventional anticonvulsant therapy, has been recommended by several authors (Janssens 1992; Durkes 1992; Panzer and Chrisman 1994; Chrisman 1995). Results of these reports are encouraging, and it is likely that acupuncture will be used with increasing frequency as an adjunctive therapy to conventional anticonvulsant therapy in dogs in the future.

Selection of an Anticonvulsant Medication

General information

The efficacy of an anticonvulsant depends on its serum concentration, because this determines its concentration in the brain (Frey 1986; Brown 1988; Schwartz-Porsche 1994). Therapeutic success can be achieved only when serum concentrations of a given anticonvulsant are consistently maintained within a therapeutic range. Therefore, anticonvulsants that are eliminated slowly must be employed. The elimination half lives of the various anticonvulsants differ considerably between different species. Few of the anticonvulsant drugs used for the treatment of epilepsy in people are suitable for use in dogs and cats. This is largely because of differences in pharmacokinetics of antiepileptic drugs in animals and in humans. Some drugs are metabolised so rapidly that it is not possible to reach consistently high serum concentrations, even with very high doses. For many drugs, pharmacokinetic data and / or clinical experience is lacking in cats, which usually metabolise anticonvulsants more slowly than dogs (Schwartz-Porsche 1994) (See Chapter 6).

Dogs

Phenobarbitone and its structural analogue, primidone, are the most efficacious anticonvulsant drugs available for use in the medical management of canine epilepsy (LeCouteur and Child 1989; Schwartz-Porsche 1994). Both drugs appear to be equally effective in the treatment of canine epilepsy, however phenobarbitone is preferred because of its lower cost and reduced adverse effects on liver function (Schwartz-Porsche *et al* 1985).

Potassium bromide is useful in dogs for the treatment of epilepsy that is refractory to phenobarbitone or primidone therapy (Trepanier 1993; Podell and Fenner 1993; Schwartz-Porsche 1994). Mephenytoin may be of limited usefulness in some cases of canine epilepsy that have proved refractory to the above mentioned drugs (Sisson 1990). Both these drugs are considered more useful as "add-on" drugs than for continued single drug therapy.

The benzodiazepines clonazepam and clorazepate have occasionally been recommended for use in dogs (Lane and Bunch 1990; Forrester *et al* 1990). Clonazepam is of limited usefulness because of the rapid development by dogs of tolerance to its anticonvulsant effects (Frey 1989). While the development of tolerance to clorazepate in dogs may be slower than that for clonazepam, physical dependence and the risk of withdrawal seizures limit the usefulness of this drug (Scherkl *et al* 1989).

There is little indication for the use of ethosuximide in dogs (Frey 1989). Based on available clinical and pharmacokinetic data, phenytoin, diazepam, carbamazepine, and valproic acid are not suitable for use as long-term anticonvulsant drugs in dogs (Frey 1989; Schwartz-Porsche 1994).

The use of slow-release phenytoin has been reported (Derkx-Overduin 1994), and results suggest that this drug may play a useful role in the management of canine epilepsy in the future.

Several new drugs may have potential usefulness in dogs or cats. Results of a clinical report of the use of vigabatrin (gamma-vinyl-GABA; a selective inhibitor of GABA-transaminase that leads to a dose dependent increase in GABA concentration in brain tissue) in dogs were encouraging (Speciale *et al* 1991), however further research is needed before this drug can be recommended for use. Another drug that shows promise for use in dogs is felbamate. Safety of felbamate has been documented in dogs at doses ranging from 15 to

300 mg/kg PO BID (Boothe 1994). Felbamate may cause an increase in phenobarbitone serum concentrations if added to phenobarbitone, and efficacy and safety of this drug in this situation have yet to be established. Other new drugs that have been considered for use in dogs are oxcarbazepine, flunarizine, progabide, gabapentin, and lamotrigine (Schwartz-Porsche 1994), however further studies will be required to determine whether any of these drugs has a place in the management of canine epilepsy.

Cats

Phenobarbitone and diazepam are the drugs best suited for the treatment of feline epilepsy (LeCouteur and Child, 1989; Schwartz-Porsche 1989; Frey 1989). Cats do not develop tolerance to the anticonvulsant effects of diazepam as is the case in dogs (Schwartz-Porsche 1989; Frey 1989).

Primidone may be used in cats (Sawchuk *et al* 1985), however, in contrast to dogs, concentrations of primidone in cats remain higher during continued treatment than those of phenobarbitone (Schwartz-Porsche 1989). Toxic adverse effects may emerge more rapidly in cats than in dogs (Schwartz-Porsche 1994).

The half-life of phenytoin in cats is very prolonged, and serum concentrations may accumulate to toxic levels (Frey 1989). Use of this drug in cats is therefore very limited. Valproic acid is unsuitable for use in cats due to its undesirable adverse effects (Dreimann 1992).

Anticonvulsant drug failure

There are many reasons for drug failure (Shell 1984; Schwartz-Porsche 1994). Improper frequency of administration or improper doses are the most frequently recognised causes of failure of a dog or cat to respond to therapy. Progression of an intracranial cause of seizures, or of an extracranial cause, may result in continued seizures. Other factors to consider when therapy fails are the development of concurrent disease (e.g. gastrointestinal disorders may alter drug absorption), occurrence of oestrus before onset of seizure activity, use of drugs that may lower the seizure threshold (e.g. phenothiazine tranquillisers), or interaction with medications that may alter serum concentrations of an antiepileptic drug. Development of tolerance to an anticonvulsant drug may result in increased seizure activity. Finally, failure to respond to anticonvulsant therapy may occur when a dog or cat is resistant or refractory to treatment with a particular agent.

Use of second anticonvulsant drug

Addition of a second anticonvulsant drug to a single agent already in use (called *combination therapy*) offers few advantages over appropriate single-drug therapy (Bunch 1986; Frey 1986; Lane and Bunch 1990). An exception to this general rule occurs in dogs that are resistant to therapy with either phenobarbitone or primidone. In such dogs the addition of potassium bromide to phenobarbitone therapy may be attempted (Schwartz-Porsche 1994). In general, however, it is recommended to begin treatment with a single anticonvulsant drug and to adjust the dosage and frequency of administration until optimal patient management is attained (Lane and Bunch 1990). Measurement of steady-state serum anticonvulsant concentrations may be necessary to achieve this goal. Only after use of a single agent has been thoroughly investigated and found to be inadequate for acceptable seizure control should an alternative anticonvulsant drug, used either alone or in combination, be considered.

Specific Recommendations for Maintenance Anticonvulsant Therapy of Epilepsy

Canine epilepsy

Generalised tonic-clonic seizures, and focal seizures, of dogs may be treated with phenobarbitone or primidone. The active principle of both drugs is phenobarbitone, however there may be dogs that respond better to primidone than phenobarbitone, and vice versa. Phenobarbitone should be regarded as the drug of first choice because it is less likely than primidone to produce hepatotoxicity (even when used in high doses for long periods), the total dose of drug needed to control epilepsy is less for phenobarbitone than for primidone, and phenobarbitone is less expensive than primidone (Schwartz-Porsche *et al* 1985).

Phenobarbitone is the drug best suited for seizure control in epileptic dogs (Schwartz-Porsche *et al* 1985; Parent 1988; Ravis *et al* 1989). Clinical reports indicate that 60-80% of epileptic dogs may be controlled effectively with phenobarbitone used as a single anticonvulsant drug (Lane and Bunch 1990). Although it is a controlled substance, phenobarbitone is a safe, effective, and inexpensive anticonvulsant drug for long term maintenance therapy.

Treatment should be started with 3-5 mg/kg/day per os divided twice or three times daily (Frey 1986). In some dogs, this dosage may result in undesirable effects such as sedation, ataxia, polydypsia, polyuria, polyphagia, and weight gain. Tolerance to these effects develops within two weeks in most dogs (Frey 1986; Lane and Bunch 1990). Occasionally "paradoxical hyperactivity" may develop, which may resolve with an increased dose or may necessitate a change in medication. Chronic use of phenobarbitone may result in moderate increases in serum concentration of enzymes commonly used to detect hepatic disease and in abnormal liver function test results, although clinical signs of hepatotoxicity rarely are seen (Dayrell-Hart 1991). Blood dyscrasias including neutropaenia rarely

have been noted. Should phenobarbitone be discontinued suddenly, withdrawal seizures may occur.

Because of the long elimination half life of phenobarbitone, steady-state serum levels will not be achieved for 10-15 days after institution of therapy or alteration of dosage (Ravis *et al* 1989). Maximum serum concentrations are reached 4-8 hours after oral administration (Lane and Bunch 1990). The time needed to reach steady-state serum concentrations may be decreased if twice the calculated maintenance dosage is given for several days (LeCouteur and Child 1989). The concept of a "loading dose" is favoured by some veterinarians, however, this practice may increase the occurrence of undesirable effects such as sedation.

In dogs in which the effect of the initial dosage is not sufficient to achieve a desired level of seizure control, the dosage may be increased in a stepwise fashion. At least 10-15 days is required to reach a steady-state after each adjustment in dosage. It may be necessary to increase dosages up to upper limits of 18-20 mg/kg/day PO divided BID or TID to decrease seizure frequency and severity to an acceptable level (Frey 1986). Increases in dosages finally are limited by occurrence of sedative effects to which tolerance does not develop.

Monitoring of serum anticonvulsant drug concentrations should be used as a guide to alterations in therapy (Brown 1988; Morton and Honhold 1988; LeCouteur and Child 1989; Schwartz-Porsche 1994). Such monitoring, however, is not a substitute for clinical judgement. Expected therapeutic serum drug concentrations are average values, and each animal will have an individual optimal value. Serum phenobarbitone concentrations may be monitored to assess response to phenobarbitone therapy. Extreme variations between oral dosage and serum concentration achieved have been reported to occur in dogs. Serum concentrations usually are between 20 and 40 µg/ml at a time when seizures are controlled or at least when frequency and severity of seizures are reduced (Frey 1986). Concentrations above 45 µg/ml have been associated with lasting undesirable effects such as ataxia or sedation in some dogs. Ideally, serum phenobarbitone concentrations should be measured 2-3 weeks after each adjustment in dosage. To determine trends in serum phenobarbitone concentrations, serum should be collected and submitted at a similar time in the daily administration cycle of phenobarbitone. It is recommended that samples be collected within one hour before the next scheduled phenobarbitone administration time.

In dogs that are not free of seizures, serum phenobarbitone concentrations should be maintained between 30 and 40 µg/ml for one to two months before the maximal effects of phenobarbitone in an individual dog may be assessed. If after this time the frequency and severity of seizures is not acceptable to the owner, then the dog may be termed refractory or therapy resistant, and alternative or additional anticonvulsant medications may be considered.

Dogs in which an acceptable level of seizure activity is maintained by means of phenobarbitone should be re-examined by a veterinarian every six months. A complete blood count, serum chemistry profile, and serum phenobarbitone determination should be completed at least annually. Appropriate dosage alterations should be considered based on results of these determinations.

Primidone undergoes hepatic oxidation to phenobarbitone and phenylethylmalonamide (PEMA) (Lane and Bunch 1990). Although primidone, phenobarbitone, and PEMA have anticonvulsant activity, it is estimated that phenobarbitone activity accounts for 80-85% of this activity (Frey 1986; Schwartz-Porsche 1994)

Clinical reports state that primidone is an effective anticonvulsant in 52-87% of epileptic dogs when used alone. This level of effectiveness is similar to that reported for phenobarbitone, however there is a much greater likelihood of hepatic or behavioural abnormalities occurring with primidone than with phenobarbitone (Lane and Bunch 1990).

A starting dosage of 55 mg/kg/day divided TID has been recommended by the manufacturers (Lane and Bunch 1990), however, lower starting dosages of 10-30 mg/kg/day divided BID or TID appear to be effective (Frey 1986). Serum phenobarbitone concentrations may be monitored to assess response to primidone therapy (Schwartz-Porsche 1994).

Bromide, a halide element, was originally introduced for use in people in the mid- to late 1800's, and was the first antiepileptic drug with any measurable efficacy (LeCouteur and Child 1989). Use of bromide in humans was largely discarded in favour of phenobarbitone after 1900, because major toxic problems (skin rashes, sedation, and behavioural changes) occurred with its use. Reports of use of potassium bromide as an anticonvulsant in dogs occurred as early as 1907 (Sewell 1907).

Bromide is an inexpensive antiepileptic drug that may be used in dogs considered to be therapy resistant to phenobarbitone (Schwartz-Porsche 1986; Sisson and LeCouteur 1990; Schwartz-Porsche 1994; Trepanier 1993; Podell and Fenner 1993). Bromide may also be considered for use in dogs with hepatic toxicity or blood dyscrasias resulting from phenobarbitone therapy, or in dogs with intolerable behavioural problems attributable to phenobarbitone (Trepanier 1993). It is rapidly and completely absorbed from the small intestine of people, however bioavailability in dogs may be more variable. Dogs fed diets high in chloride tend to have a lower bromide bioavailability (Trepanier 1993). Bromide is neither protein bound nor biotransformed, and is eliminated almost exclu-

sively by glomerular filtration. The elimination half-life in dogs is remarkably long, ranging from 23 to 60 days, depending on diet (Trepanier 1993). Bromide elimination is hastened by diets high in chloride, and so diet should remain unchanged while dogs receive bromide therapy, since differing dietary levels of chloride may alter serum bromide levels..

Bromide may be formulated as a 250 mg/ml solution of analytical grade potassium bromide (KBr) in syrup (Table 7.5) or distilled water. Potassium bromide may also be packed into gelatin capsules. Bromide may also be administered as the sodium salt in dogs sensitive to potassium (e.g. Addisonian dogs), or in dogs that dislike the taste of the potassium salt. However, when using the sodium salt the dose reported for potassium bromide should be adjusted downwards by about 15%, as sodium bromide has a higher bromide content per gram (KBr = 67% bromide; NaBr = 78% bromide) (Trepanier 1993). Note that the sodium load may be harmful to dogs with congestive heart failure, hepatic failure, or hypertension (Trepanier 1993)

The appropriate dose of bromide depends on concurrent anticonvulsants, diet, and renal function. As a second anticonvulsant, added to phenobarbitone, the initial suggested dose of potassium bromide is 22-30 mg/kg PO once daily, or divided BID (Trepanier 1993). With dogs already receiving phenobarbitone, the goal is to taper the dose of phenobarbitone to the lowest dose that controls seizures. Some dogs may be weaned off phenobarbitone completely. Bromide may be given as a loading dose to achieve therapeutic serum concentrations rapidly (Trepanier 1993). The loading dose for bromide is 400 mg/kg of potassium bromide PO in several divided doses over 24 hours, as large doses may cause nausea. Maintenance doses may be resumed in 24 to 72 hours. Loading doses may result in ataxia (Trepanier 1993).

The most frequently reported adverse effects of bromide administration in dogs are polydypsia, polyphagia, ataxia, sedation, and pelvic limb weakness (Podell and Fenner 1993). These effects are most likely to be seen when bromide is combined with phenobarbitone or other anticonvulsants. Should these signs of bromide toxicity occur, the bromide should be discontinued for at least 48 hours and resumed at a lower dosage after this time. These effects may be due to the synergistic effects of bromide and phenobarbitone, and usually respond to a 25% reduction in the dosage of phenobarbitone dose (Trepanier 1993). Other infrequently reported adverse effects of bromide are pancreatitis, increased attention seeking, aggression, coprophagia, and hyperactivity. High doses of bromide have been associated with thyroid dysfunction in humans and rats, however these effects have not yet been reported to occur in dogs (Trepanier 1993).

Because of its long elimination half life, bromide does not reach a steady state for four to six months following institution of therapy, however this will vary with chloride intake. The therapeutic range for bromide in dogs is 1000 to 2000 mg/L (Trepanier 1993). Serum bromide levels should be determined at one month, and at four to six months after initiating therapy. After a steady state is reached, bromide levels may be monitored once or twice annually, or as dictated by adverse effects. Because of the long half life relative to dosing interval, timing of blood samples with regard to dosing times is not critical as it is with phenobarbitone.

Mephenytoin - Should both phenobarbitone and potassium bromide fail to control seizures, mephenytoin may be used in addition to these two drugs, or may be used alone. Mephenytoin does not achieve therapeutic blood concentrations in dogs, however its active metabolite (nirvanol) does reach therapeutic concentrations, with a half life of 27 hours. An initial dosage of 10 mg/kg TID may be used, with the dosage increased as needed to achieve a therapeutic blood level of nirvanol of 25-40 µg/ml. Steady-state blood concentrations should be achieved in six days (Sisson 1990).

Table 7.5: *Instructions for preparation of potassium bromide (250 mg/ml) in cherry syrup*

KBr	250 gm
Cherry syrup	250 ml
Benzyl alcohol	9 ml
H_2O QS	1,000 ml

Place KBr in 1,000 ml beaker and add water (deionized or distilled) up to approximately 725 ml. Mix with magnetic stirrer until KBr is completely dissolved. Add cherry syrup and benzyl alcohol and adequate water to make one liter. May be stored at room temperature.

Mephenytoin has resulted in seizure control in a limited number of dogs refractory to phenobarbitone or potassium bromide. Dermatitis, blood dyscrasias and hepatotoxicity have been reported as complications of therapy with mephenytoin in humans (Schwartz-Porsche 1994). To date the only adverse reaction seen in dogs has been sedation, especially when the drug is used in combination with phenobarbitone or potassium bromide (Sisson 1990).

Feline epilepsy

Pharmacokinetic data regarding antiepileptic medications in cats are lacking (Frey 1986; Schwartz-Porsche 1984, 1989). At this time, only phenobarbitone and diazepam are recommended for maintenance anticonvulsant therapy in cats. Other anticonvulsant medications may be suitable for therapy in cats, however, reports of clinical experience and pharmacokinetic studies of such drugs are lacking.

Phenobarbitone - excellent clinical results have been reported in epileptic cats after phenobarbitone administration at a dosage of 3-5 mg/kg/day divided BID or TID (Schwartz-Porsche 1989). In some cats, this dosage may be increased to 10-12 mg/kg/day divided BID or TID to achieve therapeutic serum concentrations of phenobarbitone. Recommendations regarding serum phenobarbitone concentrations are the same as for dogs.

Diazepam - an alternative to phenobarbitone in cats is diazepam administered at a dosage of 0.5-2.0 mg/kg/day divided TID (Frey 1986). Effective plasma concentrations (200-500 ng/l calculated for human beings) of unchanged diazepam and its active metabolites can be maintained for years without development of tolerance to the antiepileptic effects. Some authors prefer diazepam for maintenance therapy of epilepsy in cats.

Idiosyncratic fatal hepatic necrosis has been reported as an adverse effect in cats receiving 0.5 mg/kg of diazepam for therapy of behavioural problems (Levy *et al* 1994). Affected cats became ill following eight or nine days of oral diazepam therapy, and most cats died within 24 hours despite aggressive supportive care.

Anticonvulsant Therapy for Status Epilepticus

Status epilepticus is a life-threatening cerebral event that requires prompt, aggressive treatment (Indrieri 1989). The treatment of status epilepticus focuses on stopping the seizure activity and preventing the reoccurrence of seizures, however attention must be given to other factors that are essential to the survival of the patient. These factors include ensuring patency of the airway, maintaining normal cardiorespiratory function as well as adequate tissue oxygenation and perfusion, eliminating hyperthermia and maintaining normal body temperature, and maintaining fluid, electrolyte, and acid-base balance (Indrieri 1989).

The first step in the management of a cat or dog presented during status epilepticus, or with frequent cluster seizures, is to obtain a brief history from the owner. Questions that should be included are: the age of the animal, the duration of the seizures, previous seizure history, current drug therapies (including anticonvulsants, insulin, etc.), and history of trauma or exposure to a toxin.

The next step is to initiate immediate anticonvulsant therapy. An indwelling intravenous catheter should be placed, and diazepam administered at a dosage of 0.5 to 1.0 mg/kg IV. Onset of antiepileptic action in dogs is about two to three minutes after intravenous diazepam administration (Lane and Bunch 1990). This dose may be repeated two or three times over several minutes in an attempt to stop the seizures. Generally diazepam maintains a therapeutic blood level for only about 20 minutes. A continuous intravenous infusion of diazepam may be used following the initial bolus therapy (1.0 to 2.0 mg/kg/hour for dogs, and 0.5 to 1.0 mg/kg/hour for cats, in 5% dextrose solution) (Indrieri 1989). Use of longer acting benzodiazepines such as lorazepam or clonazepam has been recommended (Lane and Bunch 1990), however it appears that the advantage of these drugs is limited to a longer duration of effect, without greater efficacy when compared to diazepam.

Should status epilepticus continue despite administration of diazepam, then therapy with phenobarbitone or pentobarbitone is indicated. Although the anticonvulsant effects of phenobarbitone are delayed in onset after administration, often by 15 to 20 minutes, greater anticonvulsant action is reported for phenobarbitone than for pentobarbitone (Lane and Bunch 1990). The recommended dosage of phenobarbitone is 2-4 mg/kg IV (Lane and Bunch 1990). This dose can be repeated IV or IM at 20-30 minute intervals until a cumulative dose of 20 mg/kg has been given (Lane and Bunch 1990). A higher loading dose of phenobarbitone of 12-16 mg/kg IV has been recommended by one author (Sisson 1990), for use in dogs that do not have a maintenance blood concentration of phenobarbitone from anticonvulsant medication given prior to admission to hospital. Following this high loading dose, the initial loading dose of phenobarbitone may be supplemented every 20-30 minutes with 2-4 mg/kg IV or IM. Upon achieving control of seizures, a maintenance dose of phenobarbitone is given (2-4 mg/kg IV or IM every six hours for 24-48 hours). If possible, oral anticonvulsant therapy should be resumed or initiated, if indicated, every 12 hours, as soon as the animal is able to swallow.

If seizure activity continues beyond 20 minutes, despite the above therapy, then pentobarbitone should be given to effect. Doses of 3 to 15 mg/kg IV are recommended for the dog, however pentobarbitone

must be given slowly, since diazepam and phenobarbitone will potentiate its effects, and marked respiratory centre depression may result. Tracheal intubation and assisted ventilation may be required following pentobarbitone administration.

Phenothiazines should be avoided in the management of status epilepticus, as their use may lower the seizure threshold.

At this stage, with the seizures controlled, cardiorespiratory function should be assessed, and the airway should be examined for any obstruction. It may be necessary to assist ventilation or to provide oxygen by means of endotracheal tube or mask. At this time auscultation of the heart is recommended, and it may be necessary to obtain an ECG tracing. Blood should be collected for a complete blood count, serum chemistry panel, blood lead determination, and other tests as deemed necessary. If possible, blood glucose level, packed cell volume, total serum protein, and serum calcium concentration should be determined immediately. Consider the administration of 25% glucose (8 ml/kg IV) or calcium gluconate (4 ml/kg IV of a 10% solution slowly) if history or results of initial blood tests suggest this action is appropriate.

Body temperature should be continuously monitored, and maintained within the normal range. If body temperature is greater than 106°F, cerebral oedema is likely to occur, and therapy for cerebral oedema must be considered. Cerebral oedema should also be suspected should the episode of status epilepticus have been prolonged prior to therapy being instituted. Animals in which cerebral oedema is suspected should be treated in the same manner as an animal suffering from head trauma (see Chapter 8). It should be remembered that fluid therapy, while essential in the face of dehydration, must be approached with care in an animal with cerebral oedema, as overhydration may worsen cerebral oedema.

Animals that have experienced a lengthy episode of status epilepticus (30 minutes or greater) may require days or weeks to recover normal function. Permanent neurological deficits may result from severe episodes of status epilepticus, however these deficits should not be assumed to have been induced by the effects of cerebral hypoxia and / or hyperthermia unless other causes are eliminated. A thorough diagnostic work-up to determine the cause of the seizures should follow stabilisation of a patient with status epilepticus.

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CHAPTER EIGHT

Diseases of the Brain

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INTRODUCTION

Diseases of the brain are some of the most devastating of all medical problems in all species. Recent advances in diagnosis and treatment of brain disease in animals have increased survivability and quality of life for many patients previously thought of having grave or terminal prognoses. Appropriate management of animals suspected to have neurological disease requires accurate lesion localisation, formulation of realistic differential diagnoses, use of pertinent diagnostic tests, and administration of beneficial therapy. This chapter emphasises the differential diagnosis of diseases of the brain in small animals. First, the response of the brain to pathological processes is described, as this has important implications for treatment and prognosis. There follows a description of the common brain diseases, grouped under the lesion location system described in Chapter 2.

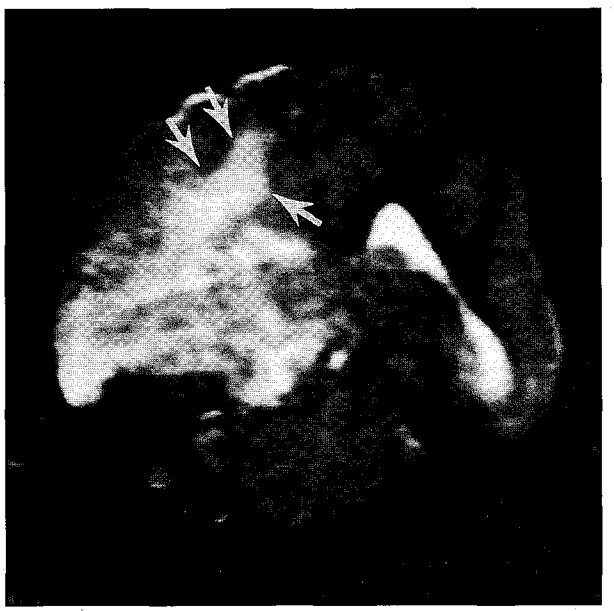

Figure 8.1: *(a) T1-weighted, contrast-enhanced (gadolinium-DTPA) and (b) T2-weighted MR images of a dog's brain. In (b), an area of increased signal intensity, consistent with oedema, is seen involving primarily the white matter of the associated cerebral hemisphere (arrows), associated with lesions seen in (a).*

PATHOPHYSIOLOGY OF BRAIN DISEASE

The brain responds to disease in a finite number of ways, regardless of the underlying primary disease process. Diseases of the brain alter normal physiological relationships by several mechanisms including, physical invasion and / or destruction of neurons, metabolic alterations in neuronal or glial cells, impairment or obstruction of the vascular supply to normal tissue (ischaemia or hypoxia), impairment of cerebrovascular autoregulation, induction of haemorrhage (intratumoural or intraventricular), irritation (seizure generation), obstruction of the ventricular system, oedema formation, production of physiologically active substances, seizure generation, and increased intracranial pressure (ICP). These pathophysiological events result in the clinical signs seen in patients.

Cerebral Oedema

Cerebral oedema is a common sequel to intracranial disease (Figure 8.1). Two major types are brain oedema are seen: vasogenic and cytotoxic. (Another type, which is less important, is interstitial oedema. This is

the transependymal movement of cerebrospinal fluid (CSF) in association with hydrocephalus.)

Vasogenic oedema

This is most often associated with intracranial tumours. It results either from vascular injury secondary to physical disruption of the vascular endothelium, or functional alterations in endothelial tight junctions. Vasogenic oedema migrates away from areas of vascular disruption via bulk flow, usually through brain white matter.

Cytotoxic oedema

This is intracellular swelling, most often the result of energy failure in cells with an associated inability to maintain transmembrane equilibrium. Ischaemia, hypoxia, and direct neuronal toxicity are causes.

Increases in intravascular pressure due to the loss of autoregulatory capacity, vascular obstruction, or hypertension perpetuate oedema formation.

Ischaemia and Hypoxia

Because normal function of neurons depends on an adequate supply of oxygen, physical disruption of blood flow can significantly impair normal brain function. Cerebral blood flow is normally maintained through a combination of systemic blood flow (pressure), and cerebral vasculature autoregulation. Autoregulation is important to maintain a near constant cerebral blood flow over a range of systemic blood pressures, and depends primarily on the $PaCO_2$ concentration of blood perfusing the brain. Diseases that alter cerebral vascular autoregulatory mechanisms make cerebral blood flow more dependent on systemic blood pressure. This results in inadequate perfusion of neurons during times of hypotension, and over-perfusion (possibly perpetuating oedema formation) during times of hypertension.

Physical disruption of cerebral vascular integrity by intracranial disease can also impair normal blood flow, resulting in ischaemia and hypoxia. Subsequent re-establishment of blood flow may also have possible detrimental effects (reperfusion injury) to spared brain, through such processes as free radical formation and lactic acid accumulation.

Haemorrhage

Haemorrhage, either within or around brain tissue, may result in rapid cerebral dysfunction, often by alteration of cerebral volume ("mass effect"). The incidence of haemorrhage associated with brain disease in dogs is poorly documented, however, head trauma, cerebrovascular disease, and tumours are possible causes. Tumours arising in association with blood vessels and rapidly growing masses are more likely to be associated with haemorrhage. Systemic coagulation abnormalities, thromboembolic diseases, and hypertension may potentiate haemorrhage. Vascular damage from therapeutic intervention (radiation therapy) may also influence the incidence of tumour-related haemorrhage.

Seizure Generation

Seizures are episodic disturbances of brain function, most often associated with disease of the forebrain (cerebral hemispheres, basal nuclei and diencephalon). As the result of brain disease, neurons may depolarise spontaneously. This will usually begin in a discrete focus of cells. Seizure activity may be confined to this initiating area (focal seizure), or spread to involve other areas of the brain (generalised seizure). Generalised seizures are most commonly seen in animals. Focal seizure activity is less common but is an important sign to recognise, as this type of seizure activity is often associated with structural brain disease.

Seizures can occur with a variety of structural and metabolic diseases of the brain. Seizures can also occur without an obvious lesion, as in the case of idiopathic epilepsy (See Chapter 7).

Increases in Intracranial Pressure (ICP)

Of the pathophysiological sequelae to brain disease, increases in ICP are responsible for much morbidity and mortality. Many of the aforementioned disease-associated abnormalities result in increased ICP as a common endpoint.

Intracranial pressure / volume relationships are expressed by the Monro-Kellie doctrine. This doctrine states that within the confines of the inelastic skull, blood, CSF and brain parenchyma normally exist in equilibrium, each maintaining a relatively stable volume and pressure. Any increase in pressure or volume of one of these components must be equally and reciprocally compensated by a change in one or both of the other components, or ICP will increase. Brain disease alters this relationship by increasing the overall volume within the intracranial space (Germon 1988).

Initially, there will be compensation for an enlarging mass within the intracranial space, thus causing minimal neuronal dysfunction. Many mechanisms are possible for such adaptation, including caudal shunting of CSF, decreasing CSF production, increased CSF absorption, decreasing arterial blood flow to the brain, and increased venous return from the brain. Of these adaptive mechanisms, movement or shifts of CSF are the most effective.

For some undefined period of time the intracranial space is compliant to this enlarging mass. As intracranial tissues become less and less compliant, progressively smaller increases in volume result in dramatic increases in ICP. Clinical signs become apparent during this time.

Clinical abnormalities resulting from increased intracranial pressure include disordered neuronal function (mental status alterations, paresis, cranial nerve

deficits, respiratory pattern alterations), and the body's attempt to compensate for the pressure elevations (hypertension, bradycardia). These clinical abnormalities are probably the result of decreased cerebral perfusion. Therapeutic intervention is often necessary to improve clinical signs and sustain neuronal function. As compliance is exhausted, shifts of brain parenchyma (herniation), resulting in severe neurological impairment and death will occur.

Effects of increased ICP

Increased ICP may impair normal neuronal function directly or result in ischaemia, trauma to cerebral vessels, haemorrhage, and / or obstruction to CSF flow. Significant elevations in catecholamines will occur to maintain cerebral blood flow. These sympathomimetics substances may predispose to secondary cardiac arrhythmias (brain-heart syndrome) (van Loon *et al* 1993). Life-threatening brain herniation is the consequence of excessively elevated ICP.

Clinical signs of increased ICP include deterioration in mental status, seizures, and paresis. Papilloedema is uncommon in dogs. Respiratory abnormalities (Cheynes-Stokes respirations, Biot's breathing) as well as cardiac abnormalities (bradycardia) may be seen. With uncontrolled ICP increases, death is common, especially when brain herniation occurs.

Brain herniation

Shifts of brain parenchyma occur commonly with intracranial tumours, and may be evidenced by the presence of mass effect on brain scans (CT or MRI). When brain herniation occurs, pressure effects are distributed to vital brain structures, often resulting in death. Types of brain herniation include subfalcial (cingulate gyrus), rostral and caudal transtentorial, foramen magnum, and herniation of brain tissue outwards through a craniotomy site (Fishman 1975). Transtentorial herniation may be evidenced by pupillary changes (cranial nerve III dysfunction). Foramen magnum herniation usually results in impaired respiration, due to pressure on respiratory centres in the caudal medulla oblongata.

Treatment of increased ICP

As increases in ICP often lead to significant clinical dysfunction, treatments that decrease ICP are desirable. Diuretics such as mannitol (1-2 gm/kg IV given over 10 minutes), potentiated with frusemide (1 mg/kg IV given after mannitol) may decrease pressures when ICP is elevated. Hyperventilation and subsequent cerebral vasoconstriction may also benefit the animal with elevated ICP by decreasing blood volume within the cranium. Corticosteroids, through reductions in cerebral oedema, may also lower ICP. Head elevation to 30° above heart level may also benefit the animal with elevated ICP.

CLINICAL SIGNS ASSOCIATED WITH DISEASE OF THE BRAIN

Methods for determining the localisation of the lesion are reviewed in Chapter 2. As many diseases preferentially affect a single area of the nervous system, accurate lesion localisation aids in formulation of the differential diagnosis.

Often, a disease will involve a focal area within the brain and will, therefore, result in localising clinical signs or neurological deficits. Because the intracranial structures are intimate and confined by the skull, changes in one area of the brain may result in damage to another associated area. For example, a localised cerebral hemispheric mass may result in increased ICP. That pressure increase is transferred to other areas within the skull, such as the brain stem. In some situations, the clinical signs resulting from the secondary pathophysiological sequelae of intracranial disease may overshadow the deficits resulting from the primary lesion, and may subsequently result in an inability to localise the primary lesion. In most instances, however, an intracranial lesion is still suspected, and regardless of lesion location, will be elucidated by advanced imaging studies.

DIFFERENTIAL DIAGNOSIS

After determination of the location of the lesion within the nervous system, a realistic differential diagnosis can be formulated. The following section discusses brain disorders commonly recognised in dogs and cats. They are listed using the DAMNIT-V formula discussed in Chapter 1. Further details of the diseases affecting cats are discussed in Chapter 14.

DISEASES OF THE BRAIN

Diseases of the Forebrain

Degenerative

Degenerative diseases can affect any part of the nervous system. Examples include multisystem neuronal degeneration of Cocker spaniels, spongiform degenerations in Labradors, Samoyeds, Silkie terriers , Dalmatians (cavitating leukodystrophy), mixed breed dogs and Egyptian Mau kittens, and multisystemic chromatolytic neuronal degeneration of Cairn terriers.

A feline spongiform encephalopathy has been seen affecting adult cats from 3 -12 years of age (Wyatt *et al* 1991). Clinical signs include ataxia and hypermetria, however, behaviour abnormalities may reflect forebrain disease.

Storage diseases are due to an inborn error of metabolism, and absence of a vital enzyme necessary to breakdown an endogenous body substance. These substances then accumulate within the neuronal or

supporting cells associated with the nervous system, eventually causing cellular dysfunction. The breed incidences and associated clinical signs of the numerous storage diseases of small animals are listed in Table 8.1 (Braund 1987). Diagnosis requires biopsy of affected tissue. Determination of lysosomal enzyme activities of brain and other body cells can provide definitive diagnosis.

Table 8.1: *Storage diseases of domestic animals.*

Disease	Enzyme Deficient/ Storage product	Breed/ Onset	Clinical Signs
Gangliosidosis GM_1			
Type 1 (Norman Landing)	Beta-Galatosidase	Beagle-cross (3 mo); domestic cats (2-3 mo) Friesian cattle(1 mo)	Tremor; incoordination; spastic paraplegia;visual impairment
Type 2 (Derry's)	Beta-Galactosidase	Simese; Korat and domestic cats (2-3 mo); Portuguese Water Dogs (5 -6mo)	Same Cerebellar
Gangliosidosis GM_2			
Type 1 (Tay-Sach's)	Hexosaminidase A	German Short-haired pointer (6-9 months)	Ataxia; incoordination visual impairment; dementia
Type 2 (Sandhoff's)	Hexosaminidase A and B	Domestic cats (2 months)	Same as with GM_1
Type 3 (Bernheimer-Seitelberger)	Hexosaminidase A	Yorkshire pigs (3 months)	Ataxia; incoordination hypermetria
Glucocerebrosidosis (Gaucher's)	Beta-Glucosidase (Glucocerebroside)	Sydney Silky dog (6-8 mo)	Same as above
Sphingomyelinosis (Neimann-Pick)	Sphingomyelinase (Sphingomyelin)	Siamese; domestic cats (2-4 mo)	Same as above (Type C); Poodle (2-4 mo)
(Six types of Nieman-Pick disease recognized in human beings (A - F) based upon age of onst, degree of hepatosplenomegaly, extent of nervous system involvment and reduction in sphingomelinase activity). Type C in cats, sphingomyelinase activity not dramatically decreased.			
Globoid Cell Leukodystrophy (Krabbe's)	Beta-Galatosidase (galactocerebrosidase)	Carin terrier; West Highland (2-5 mo); Beagle; Blue tick (4 mo); mixed; Poodle; (2 yr) Basset hound (1 -2 yr); Pomeranian (1.5 yr); domestic cat (5 -6 wk); Polled Dorset sheep (4 -18 mo)	Ataxia; incoordination; tremor, paraparesis; hypermetria;visual impairment
Metachromatic Leukodystrophy	Arylsulfatase (sulfatide)	Domestic cat (2 wk)	Progressive motor dysfunction, seizures; opisthotonus
Mucopolysaccharidosis (Maroteaux-Lamy)	Arylsulfatase B (mucopolysaccharide)	Siamese: domestic cat (4-7 mo)	Progressive paraparesis
(Hurler's)	Alpha-L-Idurondase	Domestic cat (10 mo)	Same: High incidence of meningioma in these cats
Glycoproteinosis (Lafora's)	(Glycoprotein?)	Beagle, Basset, Poodle (5 mo - 9 yr)	Depression; seizures
Mannosidosis	Alpha-Mannosidase (mannoside)	Domestic cat (7 mo); Angus; Murray Gray	Ataxia; incoordination; tremor; aggression (calves)
Gycogenesis (Pompe's)	Alpha-glucosidase	Lapland dogs (1.5 yr) domestic cats; Corriedale sheep (6 mo); Shorthorn and Brahma cattle (3-9 mo)	Incoordination; exercise intolerence
Fucosidosis	Alpha-L-Fucosidase	Springer spaniel dogs (2 yr)	Incoordination; behavorial changes dysphonia; dysphagia; seizures
Ceroid lipofuscinosis (Batten's)	Unknown	English setter (1yr); Dachshund (3.5 - 7 yr); Cocker spaniel (1.5 yr) Chihuahua, Saluki (2 yr); Australian Cattle dogs; Blue Heeler; Siamese, domestic cats (2 - 7 yr); South Hampshire sheep (6 -18 mo)	Personality change; visual impairment; ataxia; incoordination; jaw champing; seizures

Anomalous

Hydrocephalus, dilation of the ventricular system, may be either congenital or acquired (usually due to obstruction of the ventricular system by neoplasia or inflammation) (Figure 8 2). Breeds predisposed to congenital hydrocephalus include the Chihuahua, Pomeranian, and Maltese terrier. Many of these breeds, however, have ventricular dilation without related clinical signs.

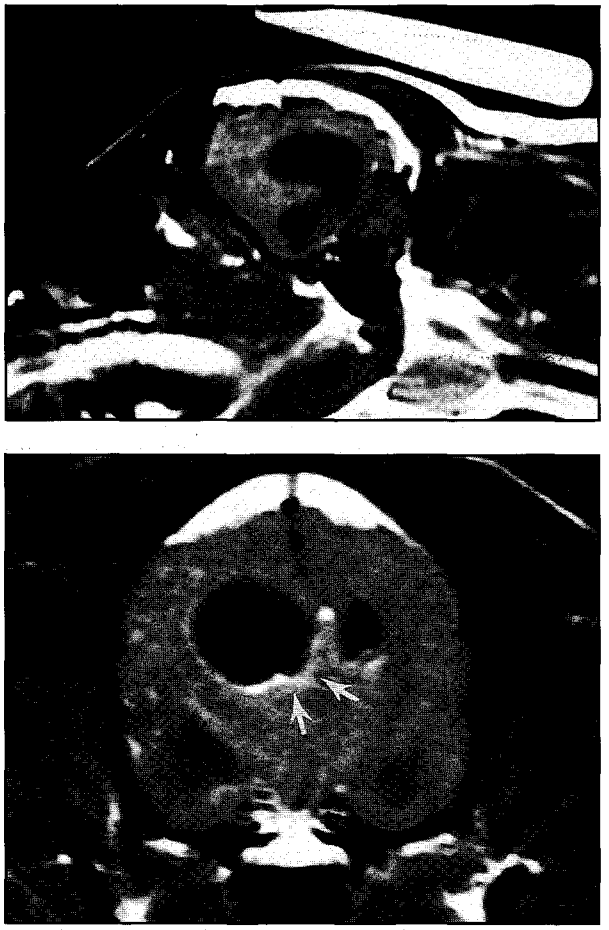

Figure 8.2: *Sagital (a) and axial (b) contrast-enhanced (gadolinium-DTPA) MR images from a dog with forebrain signs. The left lateral ventricule is dilated due to outflow obstruction at the interventricular area from a contrast-enhancing lesion (arrow). Histological diagnosis revealed a fungal granuloma.*

Congenital hydrocephalus may be due to obstruction of the ventricular system during a critical stage during development. Mentation changes and seizures are common clinical signs in animals with hydrocephalus. In Siamese cats, hereditary hydrocephalus is transmitted as an autosomal recessive trait.

Diagnosis of hydrocephalus is commonly made by brain imaging. Ventricular size can vary between breeds of dogs, and ventricular enlargement observed with these studies should be correlated with the clinical signs present. If a fontanelle is present, ultrasound may be helpful in establishing ventriculomegaly (Hudson *et al* 1990).

Medical treatments for congenital hydrocephalus include corticosteroids and diuretics to decrease CSF production. A shunt can be placed surgically to remove CSF from the ventricular system to another body cavity (e.g. the peritoneum). In instances of acquired hydrocephalus, treatment of the primary disease is imperative.

Other anomalous conditions are seen. Exencephaly - a mass of skin-covered meninges and cerebral hemispheres that project through an opening in the cranial cavity. Hydranencephaly - each cerebral hemisphere is reduced to a fluid-filled cavity. Anencephaly - lack of a cerebral hemispheres. Lissencephaly - smooth brain with no gyri and sulci, is most often seen in Lhasa Apso dogs. They are all uncommon and usually are congenital.

Metabolic

Numerous metabolic abnormalities may alter forebrain function. Liver disease (hepatic encephalopathy), renal disease (renal encephalopathy), pancreatic disease (pancreatic encephalopathy), cardiopulmonary disease, glucose abnormalities (hyper- or hypoglycaemia), electrolyte abnormalities (sodium, potassium, chloride, calcium, magnesium), and acid-base abnormalities are examples. Some of these diseases can also result in structural change within the brain. See Chapter 13.

Hepatic encephalopathy results when neurotoxins reach the brain unmetabolised, as they pass through an abnormally functioning liver (Maddison 1992). Suspected toxins include GABA, aromatic amino acids, mercaptans, ammonia, and skatoles. Animals with hepatic encephalopathy usually are admitted for seizures, ptyalism and mentation changes. Diagnosis is supported by clinical signs and abnormal liver function studies, such as elevated bile acids. In the case of a congenital portosystemic shunt, surgical correction may be curative.

Hypoglycaemia can occur secondary to insulinoma, liver disease, hypoadrenocorticism, starvation, glycogen storage diseases, and extrapancreatic neoplasia. Toy breeds and neonates may become hypoglycaemic during times of stress. Because the CNS requires a constant supply of glucose, clinical signs of hypoglycaemia relate to CNS dysfunction and include depression, seizures and tremors.

Neoplastic

Neoplasia commonly involve the forebrain, particularly in older animals.

Meningioma is the most common primary brain tumour in dogs and cats. Meningiomas arise from the arachnoid layer of the meninges and tend to occur in dolichocephalic breeds of dogs. The Golden retriever may be predisposed (Bagley *et al* 1993a).

Meningiomas are usually histologically benign, but occasionally are malignant (Figure 8.3). Solitary masses are usually seen, but in cats, multiple masses may occur. CT and MRI show a broad based, extra-axial contrast enhancing mass in most animals (Turrel *et al* 1986). CSF may be normal, inflammatory, or contain increased protein without a concurrent pleocytosis (Carrillo *et al* 1986).

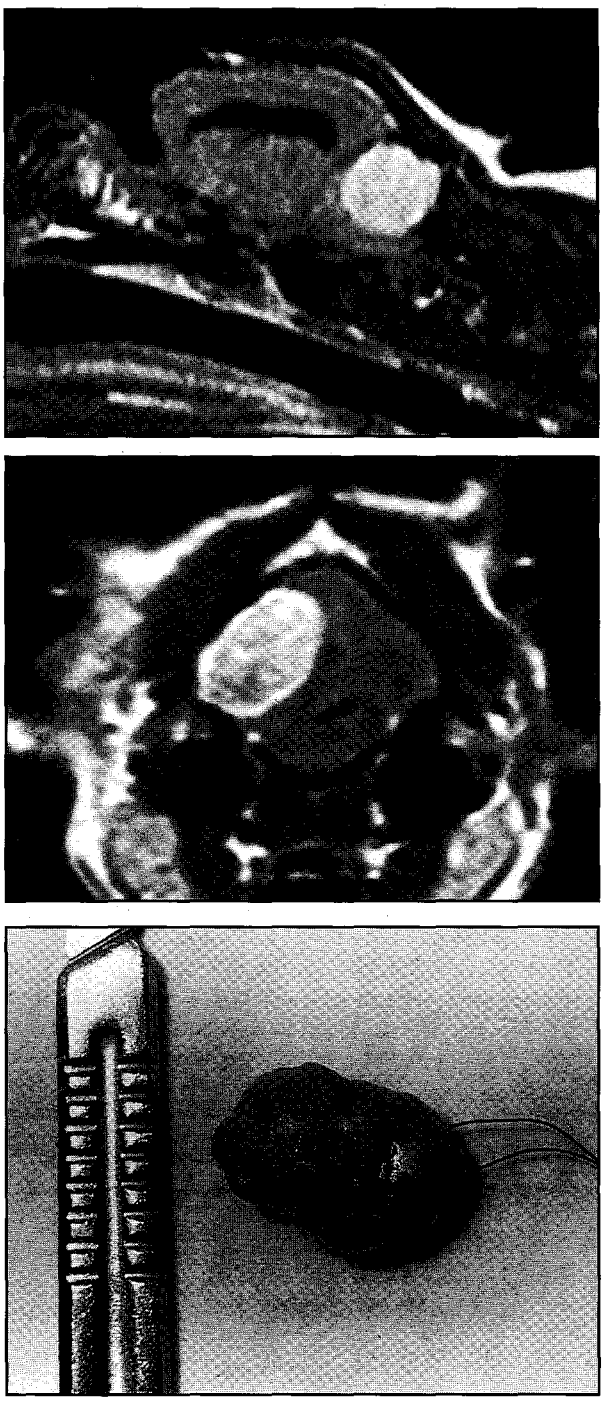

Figure 8.3: *Sagital (a) and axial (b) contrast-enhanced (gadolinium-DTPA) MRI images showing a lesion of the left cerebellar area (arrows) in a 10 year-old cat (Images courtesy of Animal Medical Imaging, Redmond, WA, USA). The lesion was removed at surgery (c). Histological diagnosis was meningioma.*

Current treatment options include surgical resection, radiation therapy and chemotherapy (Heidner *et al* 1991).

Gliomas arise from cells of the brain parenchyma. These include astrocytes, oligodendrocytes, ependymal cells, and choroid plexus cells. Brachycephalic dogs may be predisposed to development of these tumours. Choroid plexus tumours arise from areas where the choroid plexus is concentrated (the lateral, third and fourth ventricles). The CT and MRI appearance is varied and enhancement after contrast administration may not be present (Turrel *et al* 1986). CSF changes are similar to those mentioned with meningiomas. Treatment options include surgery, radiation, and chemotherapy (BCNU, CCNU) (Dimski and Cook 1990).

Pituitary tumours may result in signs of endocrine diseases (hyperadrenocorticism, acromegaly), or signs primarily related to CNS dysfunction (Sarfaty *et al* 1988). Macroadenomas may enlarge dorsally from the sella and compress the diencephalon. Treatment options include radiation and surgery.

Other primary tumours involving the forebrain are uncommon and include lymphosarcoma, germ cell tumours, dermoid and epidermoid cysts, and craniopharyngiomas.

Secondary involvement of the brain occurs via metastasis or by direct extension from extraneural sites. Numerous tumours metastasise to the brain, including haemangiosarcoma, lymphosarcoma, mammary gland and other carcinomas. Primary tumours within the nasal cavity or frontal sinuses can extent directly into the brain. Clinical signs may be localised of multifocal. CT or MRI may show single or multiple masses. With diffuse meningeal tumours these studies may be normal. Rarely CSF will reveal neoplastic cells, most commonly with lymphosarcoma and carcinomatosis.

Inflammatory

Encephalitis and meningitis often exist concurrently in dogs and cats. Clinical signs within the nervous system can be focal, multifocal or diffuse. Numerous causes have been described, which include both infectious and non-infectious diseases (Meric 1988). Incidence of infectious agents causing meningitis varies with geographic location. Most meningitis syndromes (~60 %) in small animals do not have a definable infectious cause. A **corticosteroid-responsive meningitis** seen in young, large breed dogs is thought to be idiopathic. An **eosinophilic encephalitis / meningitis** occurs without a definitive associated infectious cause in dogs and cats. Spinal cord vasculitis syndromes (Beagle pain syndrome; German short-haired pointer, and Bernese mountain dog) presenting with signs and CSF changes of meningitis have also be described.

(i) Infectious causes

Infectious agents causing brain disease include:

• **viral**	dogs - distemper, parvovirus, parainfluenza, herpes, pseudorabies, rabies, coronavirus cats - feline infectious peritonitis, feline immunodeficiency virus, feline leukaemia-associated disease
• **bacterial**	
• **rickettsial**	Rocky mountain spotted fever, Ehrlichia
• **spirochetes**	Lyme disease, leptospirosis
• **fungal**	blastomycosis, histoplasmosis, cryptococcosis, coccidiomycosis, aspergillosis, Cladosporium spp., Paecilomyces, Flavobacterium, Geotrichum
• **protozoal**	toxoplasmosis, neosporosis
• **unclassified organisms**	protothecosis

Clinical signs usually reflect multiple levels of neurological involvement. Neck pain is often found in addition to other signs or alone. Focal brain abscesses are uncommon. Fundic examination is important to assess for clues of a multisystemic problem. Imaging studies are helpful for defining structural lesions. CSF analysis is imperative for diagnosis, however, evidence of inflammation on CSF evaluation alone is not specific for meningitis, as other CNS disease (e.g. neoplasia) may result in a similar pleocytosis and protein elevation. In some instances of mass effect associated with inflammatory brain disease, CSF collection can precipitate brain herniation.

Treatment is directed at the specific cause if found. Without a definable specific cause, the author uses trimethoprim-sulphonamide antibacterials, chloramphenicol, and corticosteroids in combination. If the animal is receiving phenobarbitone, chloramphenicol should not be used, as this will shut down the metabolism of the barbiturate, leading to toxicity.

Canine distemper is caused by a paramyxovirus. Clinical signs can occur in any age of dog, regardless of vaccination status. Most commonly, young dogs with inadequate vaccinations are affected. Post-vaccinal infection may also occur. Any region of the nervous system can be involved with distemper infection. Clinical signs of a prior or concurrent systemic illness (respiratory, gastrointestinal) are not always found. Hyperkeratotic foot pads in animals with distemper indicate that CNS involvement will occur. Diagnosis is suggested by finding inclusion bodies in pathological specimens. Elevated CSF antibody titre against distemper virus is supportive of a diagnosis. Occasionally, dogs with CNS distemper do not have positive CSF distemper titres (Sorjonen *et al* 1989). No specific treatment is effective against the distemper virus. Corticosteroids, while seemingly contraindicated, may decrease inflammation and improve clinical signs in some dogs.

Feline infectious peritonitis is caused by a coronavirus infection in cats. This virus can involve various areas of the nervous system including the forebrain. Very young and very old cats are predisposed (see Chapter 14).

Toxoplasmosis most commonly affects the nervous system of cats. Dogs are infrequently affected and often will present with spinal cord dysfunction. Clinical signs depend upon the level of nervous system involvement, and include intracranial, spinal cord and lower motor neuron presentations. CSF may show a pleocytosis, usually with mononuclear cells, and occasionally eosinophils. Increasing IgG or a single positive IgM serum antibody titre are diagnostic of active infection (Lappin *et al* 1989). Treatment includes clindamycin and trimethoprim-sulphonamide drugs (Greene *et al* 1985a).

Rabies is a dramatic, but uncommon cause of CNS disease. Unvaccinated pets and those exposed to wild animals are at greatest risk.

(ii) Non infectious causes

Non-infectious diseases that can affect the forebrain include granulomatous meningoencephalitis (GME) and Pug encephalitis.

Granulomatous meningoencephalitis can occur as a disseminated disease, as a focal mass lesion, or as an ocular disease. The cause is not known. Some animals initially thought to have this disease have lymphoma. CSF usually shows a mononuclear pleocytosis. Occasionally the CSF will be normal or contain only elevated protein. CT or MRI may show diffuse inflammatory changes or a mass lesion (Figure 8.4)

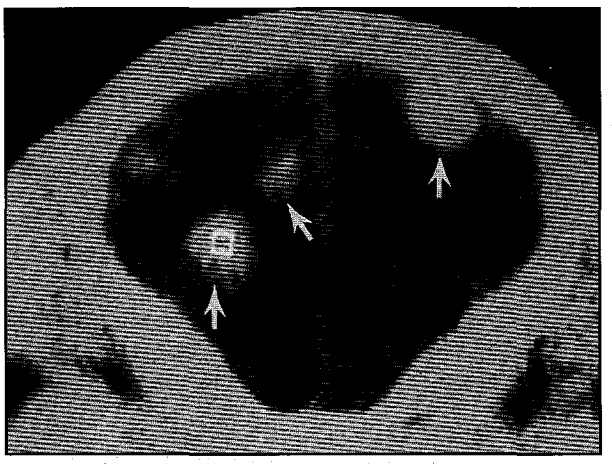

Figure 8.4: *Axial contrast-enhanced CT image of a dog with forebrain signs. Multiple focal contrast-enhancing lesions are noted (arrows). The clinical features and CT appearence were consistent with granulomatous meningoencphalitis.*

(Plummer *et al* 1992). Biopsy is needed for definitive diagnosis. Treatment options include immunosuppression (corticosteroids, azathioprine), surgery (for a focal mass), or radiation therapy. Most dogs with GME die within 6 months to 1 year of diagnosis.

Pug encephalitis occurs in young pugs and is characterised histologically by forebrain inflammation and necrosis (Cordy and Holliday 1989). This disease has been uniformly fatal, and therapy (corticosteroids) has not altered the course of the disease. A similar disease has recently been described in Maltese terriers (Van Winkle *et al* 1992).

Idiopathic

Idiopathic epilepsy is recurrent seizures without an underlying cause. Seizures in animals with idiopathic epilepsy begin between 6 months and 4 years of age. Certain breeds of dogs may be predisposed, and a hereditary basis is proven in some animals and suspected in others. Seizures are typically of a grand mal type. Diagnostic testing is normal but necessary to rule out other causes of seizures. Treatment is initially begun with phenobarbitone. See Chapter 7 for full discussion.

Narcolepsy (excessive daytime sleepiness) and ***cataplexy*** (periods of acute muscular hypotonia) usually occur without underlying structural brain disease. The actual anatomical or physiological abnormality may lie within the brain stem, however, clinical signs usually reflect a cerebral disturbance. Rarely, a structural brain abnormality is found. Abnormal neurotransmitter metabolism, possibly within the reticular activating system are thought to be responsible. Breeds of dogs predisposed include the Doberman, Labrador retriever, Miniature poodle, Dachshund, Beagle and Saint Bernard. Clinical signs usually begin at a young age, however, dogs as old as 7 years have been diagnosed with this disease. Acute onset of REM sleep, usually occurring with stimulation such as eating, is characteristic of narcolepsy.

Physostigmine (0.025 - 0.1 mg/ kg IV) potentiates the attacks for up to 45 minutes. The tricyclic antidepressant imipramine, which potentiates serotonin, may be helpful as both a diagnostic test and as therapy for narcolepsy. See Chapter 13.

Springer spaniel rage syndrome occurs in young to middle age Springer spaniels. These animals become aggressive, usually toward people in the household. No pathological lesion has been found to explain this behaviour change. Treatment is with behaviour modification.

Other bizarre behaviours such as tail chasing and flank sucking are occasionally attributed to forebrain abnormalities. However, proof of a intracranial cause in often lacking.

Traumatic

Head trauma can result in forebrain signs due to haemorrhage, oedema, contusion, penetrating wounds, or depressed skull fractures. Diagnosis is usually straight forward if the traumatic incident is witnessed. Treatment centres around control of ICP and cerebral oedema. Surgical decompression of compressive skull fractures or sub-dural haematoma may be indicated.

Toxic diseases

Numerous toxins can affect the nervous system, either primarily or secondarily. Examples of primary toxins include organophosphates, metaldehyde, lead, bromethalin, and hexachlorophene.

Lead toxicity can damage cerebral capillary endothelium within the brain, resulting in haemorrhage and oedema. Young dogs are more likely to ingest lead because of their indiscriminate eating habits. Cats are rarely affected. Inappropriate increases in the nucleated red blood cell count and basophilic stippling on haematology may be a clue of lead toxicity. Whole blood lead concentrations may support the diagnosis. Treatment of lead toxicity includes removal of the source of lead and in vivo chelation of the metal with calcium EDTA.

Vascular

Vascular disease involving the forebrain is uncommon in animals, compared with the high prevalence in human beings (Joseph *et al* 1988). Thrombosis, infarction and haemorrhage can occur in the following circumstances:-

- spontaneously
- secondary to drug therapy (L-asparaginase, anticoagulants)
- with thrombocytopenia and other bleeding disorders;
- with trauma
- with hypertension
- with atherosclerosis from hypothyroidism
- with infection (e.g. septic emboli with bacterial endocarditis).

Clinical signs are usually acute in onset, and may be initially progressive as the vascular event results in secondary brain disease and oedema. Haemorrhage and infarction may be seen with CT and MRI. Treatment of the primary haemorrhage is usually not feasible. Management of the secondary pathophysiological sequelae such as oedema and increased ICP may be helpful.

Feline ischaemic encephalopathy (cerebral ischaemic necrosis) is an ischaemic necrosis of the cerebral hemisphere of cats. The distribution of the infarction is usually in the area supplied by the middle cerebral artery. Vascular lesions, however, are infrequently found at necropsy. Clinical signs usually reflect a

unilateral forebrain abnormality. CSF often contains mild elevations in protein. Computed tomography and MRI abnormalities have not been described. Prognosis for life is good after the first 48 hours as this is a non progressive disorder. Residual neurological deficits may persist. See Chapter 15.

Parasitic

Parasites most commonly affect the forebrain during aberrant migration. Examples include Toxocara, heartworm and Cuterebra larva. Treatment is directed at parasite removal. Anthelmintics are rarely effective when the CNS is involved.

Diseases of the Brain Stem

Many of the same diseases that affect the forebrain can also affect the brain stem and cerebellum. Some of the more important disease of the brain stem are described below.

Degenerative

Storage diseases are described in Table 8.1.

Metabolic

Metabolic disease can result in depression of sensorium, which may indicate a brain stem (reticular activating system) or cerebral cortical disease. Causes of metabolic encephalopathy are discussed under forebrain diseases.

Neoplastic

Both primary and metastatic neoplasia can involve the brain stem. Meningiomas (en plaque) can lie along the floor of the skull and result in brain stem compression. Choroid plexus tumours commonly involve the fourth ventricle, resulting in signs of vestibular dysfunction.

Nutritional

Thiamine deficiency is the most common nutritional deficiency affecting the central nervous system and is seen most often in cats. Deficiency of this vitamin results in lesions in the oculomotor and vestibular nuclei, the caudal colliculus and lateral geniculate nucleus. The earliest clinical sign is vestibular ataxia, progressing to seizures, ventral neck flexion and dilated, non-responsive pupils. Treatment is by administration of thiamine.

Inflammatory

Inflammatory disease may affect the brain stem as part of their multifocal distribution. Diseases similar to those that can affect the forebrain are seen. Rocky Mountain spotted fever commonly involves the brain stem, particularly the vestibular system (Greene *et al* 1985b). Diagnosis is based on lack of mass lesion on imaging and pleocytosis on CSF evaluation. Usually there is a history of systemic illness (usually with thrombocytopenia) 7 to 10 days prior to development of neurological signs. Treatment with tetracycline, doxocycline and / or chloramphenicol is usually effective, however, residual neurological signs due to associated damage may persist even after the primary organism is removed.

Trauma

Evidence of brain stem trauma usually suggests a poorer prognosis for recovery than in forebrain trauma alone. Brain stem function can be assessed by evaluation of cranial nerve function, particularly the oculovestibular response. Occasionally, dogs have brain stem signs with cranial cervical lesions, therefore, manipulation for the oculovestibular response should be made only after assessing for unstable cervical fracture or luxations.

Vascular

Vascular diseases similar to those described under forebrain diseases may involve the brain stem.

Diseases of the Cerebellum

The cerebellum may also be affected by many of the intracranial disease processes already mentioned in the previous sections of this chapter. Additional diseases that primarily affect the cerebellum or result in clinical signs similar to cerebellar dysfunction are described below.

Degenerative

Cerebellar abiotrophies result from loss of a vital substance necessary for continued vitality of the neuron and are seen most notably in the Kerry blue terrier, Gordon setter, Rough collie, Border collie, Bull mastiff, and rarely in Samoyeds, Airedales, Finnish harriers, Labrador retrievers, Golden retrievers, Beagles, Cocker spaniels, Miniature poodles, Cairn terriers and Great Danes (deLahunta 1980). In Gordon setters and Brittany spaniels, a late onset cerebellar degeneration has been described (Steinberg *et al* 1983, LeCouteur *et al* 1988). The age of onset of clinical signs is between 6 -30 months in Gordon setters, and between 7 and 13 years in Brittany spaniels.

Storage diseases can result in cerebellum degeneration (Table 8.1). Clinical signs are of a progressive cerebellar disease. Diagnosis is based upon biopsy or necropsy. No treatment is effective in most instances.

Many cats with FSE will present with ataxia, indicating cerebellar involvement. However, most have signs indicating more diffuse disease - see above.

Anomalous

Hypomyelination or dysmyelination is discussed here as the clinical signs may mimic cerebellar disease (Duncan 1987). Breeds affected include the Chow chow, Springer spaniel, Samoyed, Weimaraner, and Bernese mountain dogs. This disease is inherited as an X-linked trait in Springers. Individual cases have been reported in a Dalmatian and a mixed breed dog. Abnormal oligodendrocyte numbers or function is the sug-

gested pathogenic mechanism. Clinical signs consist of tremor, which may appear to be cerebellar in origin. This tremor usually worsens with excitement. Tremor usually begins in affected dogs in the first few months of life and is most commonly a generalised tremor, which may distinguish itself from the predominant intention tremor of the head seen with cerebellar disease. Diagnosis is based upon clinical signs and signalment. Ante mortem diagnosis requires brain biopsy. No treatment is helpful, but spontaneous improvement occurs in Chow chows and Weimaraners.

Neuroaxonal Dystrophy is seen in Rottweilers (Chrisman 1986), and also in Collies, Chihuahuas, and domestic cats. In Rottweilers, it is characterised by cerbellar signs (ataxia, hypermetria, loss of menace response, head tremor) beginning at 1 to 2 years (ataxia), and progressing over the next 2 to 4 years (menace deficits, intention tremor). Conscious proprioception remains intact. There is no treatment.

Leukoencephalomyelopathy has been seen in two young Rottweilers (Chrisman 1986) with progressive ataxia and weakness. No clinical dysfunction is noted in the head, even though pathologically the deep cerebellar white matter is abnormal (demyelination). Clinical signs suggest a spinal cord problem. Diagnosis is confirmed at necropsy.

Congenital malformations of the cerebellum are occasionally seen. Caudal vermian hypoplasia is described, with some dogs having associated ventricular dilation (Dandy Walker malformation) (Kornegay 1986).

Cerebellar hypoplasia has been recognised in Chow chows, Irish setters and Wire-haired fox terriers. The latter two breeds may have concurrent lissencephaly.

Cerebellar aplasia has been reported in Siberian huskies.

Feline cerebellar hypoplasia is caused by intra utero infection with the panleukopenia virus (parvovirus), which affects the external germinal layer of the cerebellum and prevents the formation of the granular layer. Some affected cats have a concurrent hydrocephalus and hydranencephaly. The clinical signs are of a diffuse cerebellar disease. The course is non progressive. Diagnosis can be aided by history and clinical signs.

Neoplasia

Primary or secondary neoplasia involving the cerebellum is uncommon. Medulloblastoma is a primary brain tumour that occasionally involves the cerebellum in dogs.

Inflammatory

Generalised Tremor Syndrome or White Shaker Dog syndrome is another tremor disorder that may be associated with cerebellar disease. Affected dogs present with diffuse, fine, whole body tremor and other signs that can resemble cerebellar abnormality. Dogs with white hair coats (Maltese terrier, West Highland white terrier) are more commonly seen, but dogs with other coat colours may also be affected (Farrow 1986). Additional neurological abnormalities include nystagmus, menace response abnormalities, proprioceptive deficits, and seizures. This syndrome is most often the result of a mild lymphocytic encephalitis. No causative agents have been established to date. CSF is usually abnormal containing a mild lymphocytic pleocytosis. Protein concentration may be normal or mildly increased. Occasionally, CSF analysis is normal. Computed tomography has been reported in only a few cases.

In one group of Maltese terriers with this disease, ventricular enlargement was seen in some on CT scan, but the significance of this is unclear (Bagley *et al* 1993b). Affected dogs generally respond to immunosuppressive dosages of corticosteroids. Gradual tapering of the dose should be performed to prevent recurrence. Relapse is possible, and corticosteroids may be required for the life of the animal to control clinical signs.

Vascular

Rarely, thromboembolic and vascular diseases involve the cerebellum (Bagley *et al* 1988).

Specific Cranial Nerve Problems

See also Chapter 2.

Cavernous sinus syndrome (CNs III, IV, and VI)

With lesions of the cavernous sinus (venous structure that lies on the floor of the skull and encircles the pituitary gland), abnormalities of CNs III, IV, VI, the ophthalmic branch of CN V, and the sympathetic input to the eye may be seen (Lewis *et al* 1984). Causes include neoplasia and granulomatous disease. Ancillary diagnostic tests that may help in defining the disease include CT, MRI and cavernous sinus venography. CSF analysis may reveal neoplastic cells when diffuse neoplastic diseases such as lymphosarcoma are involved.

Trigeminal nerve disease (CN V)

Trigeminal nerve abnormalities occur with infiltrating neoplasia that involve a branch or the entire nerve. Lymphosarcoma and monocytic leukaemias are often associated with these palsies. Other cranial nerves (VII) and the sympathetic system may be involved concurrently (Carpender *et al* 1987).

Trigeminal neuritis is an idiopathic inflammatory disease of the mandibular branches of both CNs V.

Dogs present with a dropped jaw and inability to close the mouth. The aetiology is unknown. Most dogs improve within 2 - 4 weeks. No treatment has shown any benefit.

Rarely, nerve sheath tumours may arise on the trigeminal nerve. Clinical signs usually reflect a unilateral disorder.

A sensory trigeminal neuropathy has been reported in a young Collie dog (Carmichael and Griffiths 1981). Clinical signs included excessive salivation, coughing and dysphagia. No cause was found for the disease.

Facial nerve (CN VII)

Facial paralysis is the most common abnormality seen with facial nerve disease. This can occur as an idiopathic condition, as a result of otitis media / interna, trauma, and tumour of the middle ear. Hypothyroidism is associated with this condition in some dogs. Hyperinsulinism (islet cell tumour) and other metabolic abnormalities are also rarely associated. Trauma may affect only one branch of the nerve.

Hemifacial spasm is suspected to be due to hypersensitivity of the facial nerve. Otitis media / interna and tumour of the middle ear are other possible causes. The disorder may also be idiopathic in dogs.

Vestibulocochlear nerve (VIII)

Idiopathic peripheral vestibular disease occurs in both dogs and cats. Older dogs (canine geriatric vestibular disease), and young to middle aged cats (feline idiopathic vestibular disease) are most commonly affected. No cause is defined. Clinical signs are of an acute peripheral vestibular disorder with nystagmus (horizontal or rotary), head tilt (toward the side of the lesion), rolling and falling. No other neurological signs are seen. Clinical signs usually improve in 1 to 2 weeks. The nystagmus usually resolves quickly whereas a mild head tilt may remain. No treatment has proved beneficial. Recurrence is possible.

If Horner's syndrome or facial nerve paresis are also found, other causes of middle / inner ear disease should be considered. Differential diagnosis of peripheral vestibular disease include otitis interna in dogs and cats, middle ear polyps in cats, and neoplasia (squamous cell carcinoma of the middle ear) in both species. Otoscopic examination, bulla radiographs, advanced imaging studies (CT, MRI), or exploratory surgery may be needed to confirm the diagnosis.

Congenital peripheral vestibular disease is seen in several breeds including German shepherd dogs, Dobermanns, English cocker spaniels, Siamese and Burmese cats. Bilateral congenital vestibular disease is seen in Beagles and Akitas. Clinical signs include head tilt, ataxia and in some, deafness. With bilateral disease, a normal physiological nystagmus is not elicited. The head may be held low with wide exclusions from side to side. Signs may remain persistent throughout life or may improve spontaneously. There is no treatment.

Congenital deafness is found in a number of breeds including the Dalmatian, Australian heeler, English setter, Australian shepherd dog, Boston terrier, Old English sheep dog, and English bulldog (Holliday *et al* 1992). Most studies have found degeneration or hypoplasia of the organ of Corti, spiral ganglion, and cochlear nuclei. One study has suggested that this may begin as a temporal lobe (auditory cortex) problem (Ferrara and Halnan 1983). Diagnosis can be made subjectively by loss of Pryor's reflex, or objectively by brain stem auditory evoked potential testing. No treatment is effective.

Toxicity with metronidazole may result in central vestibular signs, usually associated with high doses of the drug (Dow *et al* 1989). Clinical signs suggest central vestibular disease. Discontinuation of the drug is imperative. Some dogs may die, while other will recovery completely. Aminoglycosides, administered either systemically or topically, may cause deafness and vestibular signs.

Tumours of the caudal fossa, such as choroid plexus tumours and meningiomas may cause vestibular signs. Other clinical signs suggestive of the central vestibular origin of the problem (e.g. paresis) are not always seen.

Cranial nerve IX and X disease

Disease of CNs IX and X result primary in dysphagia and laryngeal / pharyngeal problems. Dysphagia may be seen with myopathy, peripheral neuropathy, and neuromuscular junction disease. Central causes are rare, but disease involving these cranial nerve nuclei may result in dysphagia. Hydrocephalus, tumours and inflammatory diseases are possible.

DIAGNOSTIC TESTS FOR INTRACRANIAL DISEASE

After establishment of an appropriate differential diagnosis list, diagnostic tests are chosen to allow definitive diagnosis.

If a structural brain disease if suspected, an advanced imaging study (CT or MRI), and CSF analysis are indicated (Chapters 4 and 5). If CT or MRI shows an obvious structural lesion, CSF should be collected with caution because of the possibility of associated increases in intracranial pressure. As CSF alone rarely yields a definitive diagnosis, and because of the associated risks, collection of CSF should not be performed in animals at risk of brain herniation.

Electroencephalography (EEG) may be helpful in evaluation of non-structural encephalopathy and seizure focus localisation, however, often this tests provides no additional information than that provided by imaging studies and CSF analysis (Chapter 4).

Brain stem auditory evoked potential (BAEP) testing often is used to determined deafness and may provide information about brain stem integrity.

Often, surgical biopsy may be necessary for definitive diagnosis of an intracranial abnormality.

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CHAPTER NINE

Abnormalities of Eyes and Vision

Simon M. Petersen Jones

INTRODUCTION

This chapter is divided into two parts:-

PART 1 - A suggested routine for a neuro-ophthalmological examination.

PART 2 - Neuro-ophthalmological problems considered by the following presenting signs:-

Section I Loss of vision
Section II Differences in pupil size - Anisocoria
Section III Disorders affecting eye position and eye movement
Section IV Abnormalities of blink
Section V Disorders of lacrimation with a neurological basis

The sections are intended to be a guide to the investigation of each presenting sign, rather than an exhaustive dissertation on each subject.

PART 1 NEURO-OPHTHALMOLOGICAL EXAMINATION

Clinical History and General Clinical Examination

A full clinical history should be taken and a complete physical examination performed as part of the investigation of every animal presenting with a neuro-ophthalmological problem.

Neuro-ophthalmological Examination

Table 9.1 lists the cranial nerves that influence the eye and their functions. Table 9.2 lists the equipment required for a full neuro-ophthalmological examination. A set routine should be used to ensure that no abnormalities are overlooked.

Initial "Hands-off" Examination

Initial observations of the patient before it is restrained can be very useful. An impression of general mental awareness is gained and an assessment of vision made. The presence of abnormalities such as a head tilt or nystagmus can be detected.

Vision Testing

The extent to which the vision of animals can be assessed is limited, and the results of vision tests need careful interpretation. Attempts should be made not only to show the presence or absence of vision, but also to assess the extent of vision loss and the portion of the visual field affected (e.g. medial or lateral field of each eye). Tests commonly used include the ability to negotiate obstacle courses; the ability to track objects visually (e.g. the cotton wool ball test); and the menace response.

Obstacle course

Obstacle courses are very useful in dogs. The owner and dog are positioned with an obstacle course between them (Figure 9.1). The owner calls the dog and the ability of the animal to negotiate the obstacles is observed. This test can be repeated with each eye blindfolded in turn (Figure 9.2). Obstacles are moved between tests so the dog does not learn their position. The test should be repeated under dim lighting, as reduced night vision may be an early sign of conditions such as generalised progressive retinal atrophy.

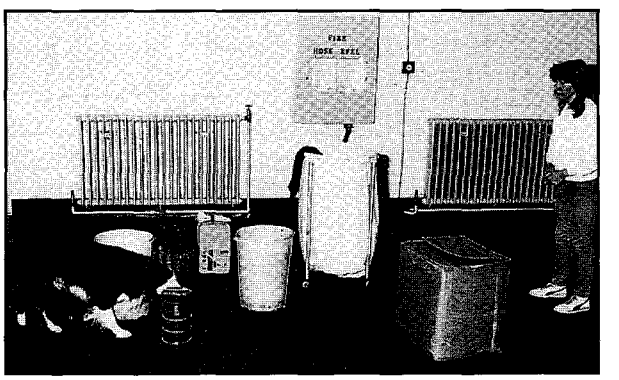

Figure 9.1: A dog with one eye blindfolded negotiating an obstacle course.

Menace test

Each eye is tested individually whilst the other eye is covered by a hand. Attempts should be made to assess the medial and lateral visual fields of the same eye. This response is present from about four to six weeks of age.

Table 9.1: Cranial nerves influencing the globe and adnexa.

(a) Sensory (afferent) nerves:-

Type of nerve supply	Nerve(s) involved	Sensory function
General somatic afferent	Trigeminal nerve (V) (predominantly ophthalmic branch)	Globe and adnexa (touch, pain, temperature etc.)
Special somatic afferent	Optic nerve (II)	Vision

(b) Motor (efferent) nerves:-

Type of nerve supply	Nerve(s) involved	Motor function
General somatic efferent	Oculomotor nerve (III) Trochlear nerve (IV) Abducens nerve (VI)	Levator palpebrae superioris muscle and extraocular muscles
General visceral efferent a) Parasympathetic branch	(i) Within oculomotor nerve (III) (ii) Within facial nerve (VII)	Pupillary constrictor muscle Secretory control of lacrimal gland
b) Sympathetic branch	Pass via thoracolumbar outflow (T_1-T_3) and vagosympathetic trunk	Pupillary dilator muscles and smooth muscles within orbit and eyelid
Special visceral efferent	Facial nerve (VII)	Muscles of facial expression

Table 9.2: Suggested facilities/equipment for examination.

1. Room capable of being darkened.
2. Area in which obstacle course may be constructed.
3. Obstacles for obstacle course (e.g. chairs, litter bin, etc.).
4. Bandage to use as a blindfold.
5. Focal light sources - such as pen torch.
6. Ophthalmoscope (direct and, if available, indirect).
7. Mosquito artery forceps for testing skin sensation.
8. Wisp of cotton wool for testing corneal sensation.
9. Schirmer tear test strips.
10. Drugs:-

    Tropicamide 1% drops - a parasympatholytic pupillary dilator (for examination of lens and fundus)

    Pilocarpine 1% drops - a direct acting parasympathomimetic (pupillary constrictor)

    Physostigmine 0.5% drops - an indirect parasympathomimetic

    Phenylephrine 10% drops - a direct acting sympathomimetic (pupillary dilator) .
11. Further equipment may be desired for ophthalmological examination (e.g. goniolens, magnifying loupes, slit lamp, etc.)
12. Specialised equipment for measuring electroretinogram, evoked visual potentials.

Figure 9.2: *A dog with one eye blindfolded.*

Figure 9.3: *The menace response. A threatening gesture is made within the animal's field of vision, which should result in blinking and possibly withdrawal of the head. Care must be taken not to create air currents, which are felt on the cornea and thus cause the animal to blink.*

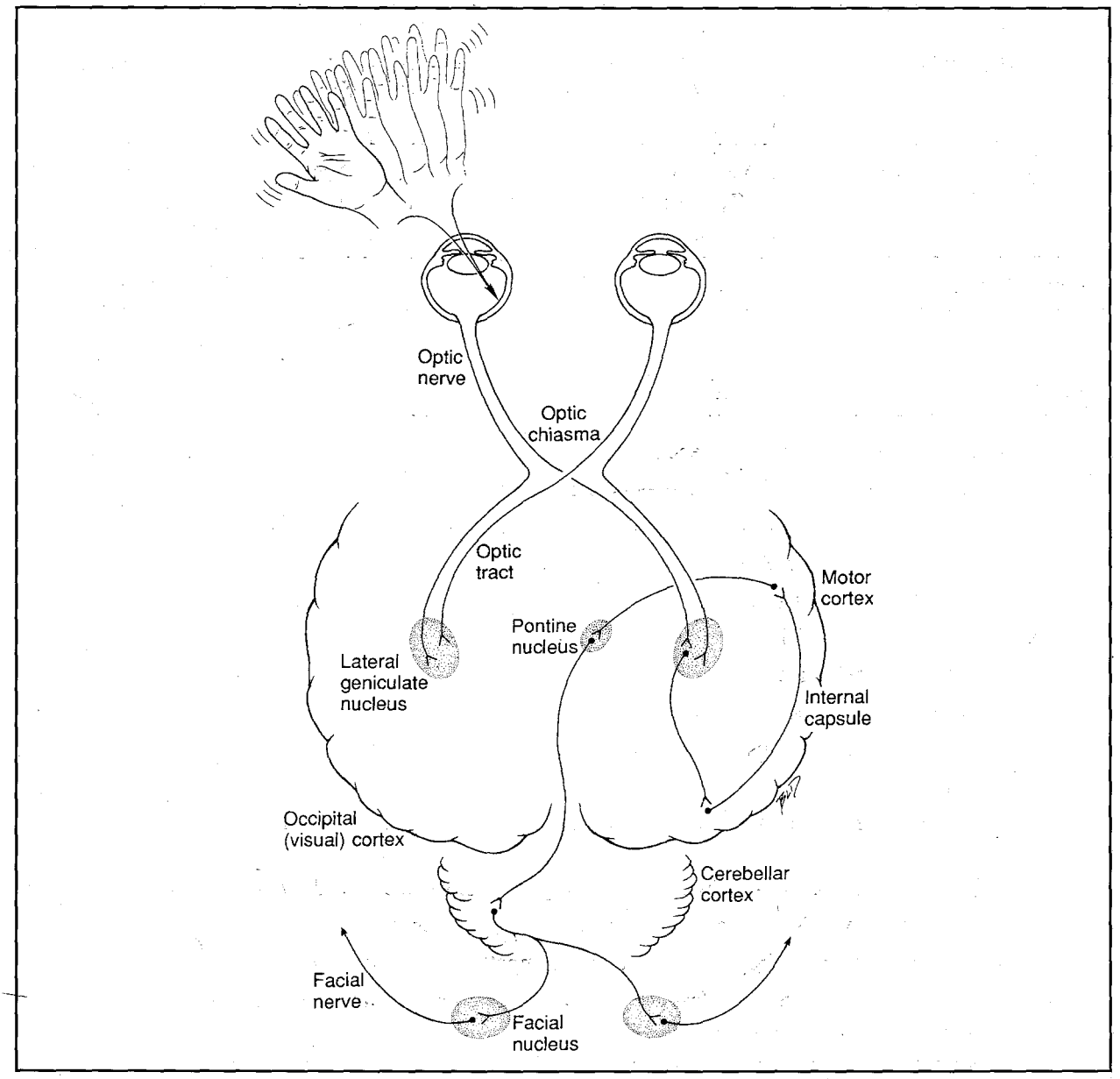

Figure 9.4: *Schematic representation of the pathways involved in the menace response.*

Cotton wool ball test

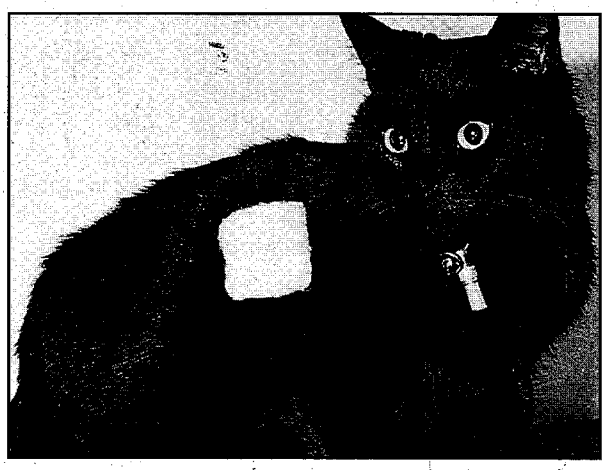

Figure 9.5: The cotton wool ball test. The cotton wool ball is thrown across, or swung across the patient's visual field (on a thread), and the reaction noted. The animal should not be restrained while this test is performed.

Pupillary Reactions

An evaluation of the briskness and completeness of the pupillary responses should be made. (Note that pupillary responses are often slow when an animal is first examined, but as it relaxes they should improve). A bright pen torch or transilluminator should be used. Abnormalities of pupillary response may result from intraocular disease as well as from neuro-ophthalmological disorders.

Comparison of pupil size

The sizes of the pupils are compared (Figures 9.6 and 9.7). The ability of the pupils to dilate fully and evenly in darkness should be checked.

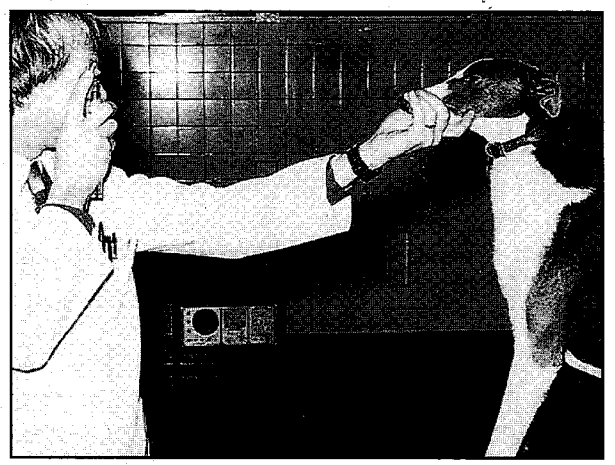

Figure 9.6: Performing distant direct ophthalmoscopy.

Pupillary light reflex (PLR)

A light is shone into each eye in turn and the direct PLR (ipsilateral pupillary constriction) and consensual PLR (contralateral pupillary constriction) of each eye is observed. In cats and dogs the direct PLR is slightly greater than the contralateral response, but this difference may be difficult to appreciate. When a constant light is shone into an eye, the pupil aperture does not remain exactly fixed; slight alterations in size normally occur.

The "swinging flashlight" test

This is a slightly more elaborate way of assessing the PLR. A light source is shone into one eye and the reaction of the pupil noted. The light is quickly swung across to the other eye and the second pupil is seen to constrict slightly, or stay at approximately the same aperture.

"Cover test"

The animal is positioned in an evenly lit room and each eye covered in turn. The response of the pupil of the contralateral eye is noted. The pupil size should not alter significantly when the opposite eye is covered.

Eyelid Position, Eye Position and Movement

The size of the palpebral openings, position of the third eyelids and of the globes is noted.

Normal nystagmus and the oculocephalic reflex

Nystagmus is an involuntary rhythmical eye movement with a slow and fast phase. Usually the slow phase is a movement of the eyes from their central position; the eyes are then rapidly re-centred by the fast phase. Nystagmus is described by the direction of the fast phase.

Nystagmus can normally be induced by the oculocephalic reflex. This is performed by turning the head laterally (or moving it in a dorsoventral plane). While the velocity of head movement is changing,

Figure 9.7: A dog's pupils viewed by distant direct ophthalmoscopy.

nystagmus is induced. Initially the eyes turn in unison in the opposite direction to the direction of rotation, and then rapidly re-centre within the palpebral opening. The process is repeated several times. The speed

of the slow phase of the nystagmus matches the speed of rotation of the animal. After the head has stopped moving the nystagmus stops; if it continues this is abnormal.

The clinician should also look for spontaneous (abnormal) nystagmus, either when the head is held in a normal position or when it is moved to abnormal positions.

Nystagmus induced by the oculocephalic reflex is mediated by the vestibular system and does not require visual input.

Other forms of normal nystagmus

Higher centres also influence eye movement; the autonomic "pursuit" eye movements co-ordinated by the cerebral cortex allow fixation on moving objects (or a stationary object if the head is moving). Nystagmus induced when looking out of the window of a moving train, for example, is a result of this system. It is called opticokinetic nystagmus and requires an intact central visual pathway.

Sensation

Normal sensory innervation to the eyelids and ocular surface should be checked using the palpebral and corneal blink reflexes.

The corneal blink reflex (Figure 9.8) may be tested using a wisp of cotton wool, taking care not to touch the eyelids (their main sensory innervation is via the maxillary branch of the trigeminal nerve as opposed to the ophthalmic branch for the cornea) or allow the animal to see the cotton wool approaching (this may induce a blink due to the menace response). An aesthesiometer has been used to assess canine corneal sensation. Not surprisingly, brachycephalic breeds of dog have less sensitive corneas than other breeds (Barrett *et al* 1991).

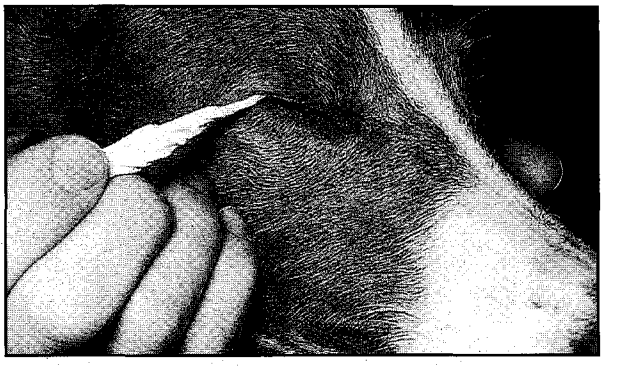

Figure 9.8: *Testing corneal sensation (corneal reflex) with a wisp of cotton wool.*

Motor Innervation

The motor innervation to the eyelids should be checked by inducing a blink by either the corneal, palpebral or menace tests.

Detailed Ophthalmological Examination

This examination should be performed in a darkened room. A focal light source and ophthalmoscope are required. It is normal to start at the adnexa and work systematically towards the caudal parts of the eye. This is well described elsewhere (Mould 1993). Note that certain parts of the examination must by necessity be performed before others, for example, pupillary reactions must be assessed before a mydriatic drug is used; measurement of tear production (Schirmer tear test) should be performed before the eye is moistened by any drops etc.

Specialist Examinations

These include electroretinography, measurement of visual evoked potentials and electromyography. Brain scanning (CT or MRI) can also be of use in particular patients.

PART 2
NEURO-OPHTHALMOLOGICAL PROBLEMS

ECTION I
LOSS OF VISION

The central visual pathways are shown in Figure 9.9.

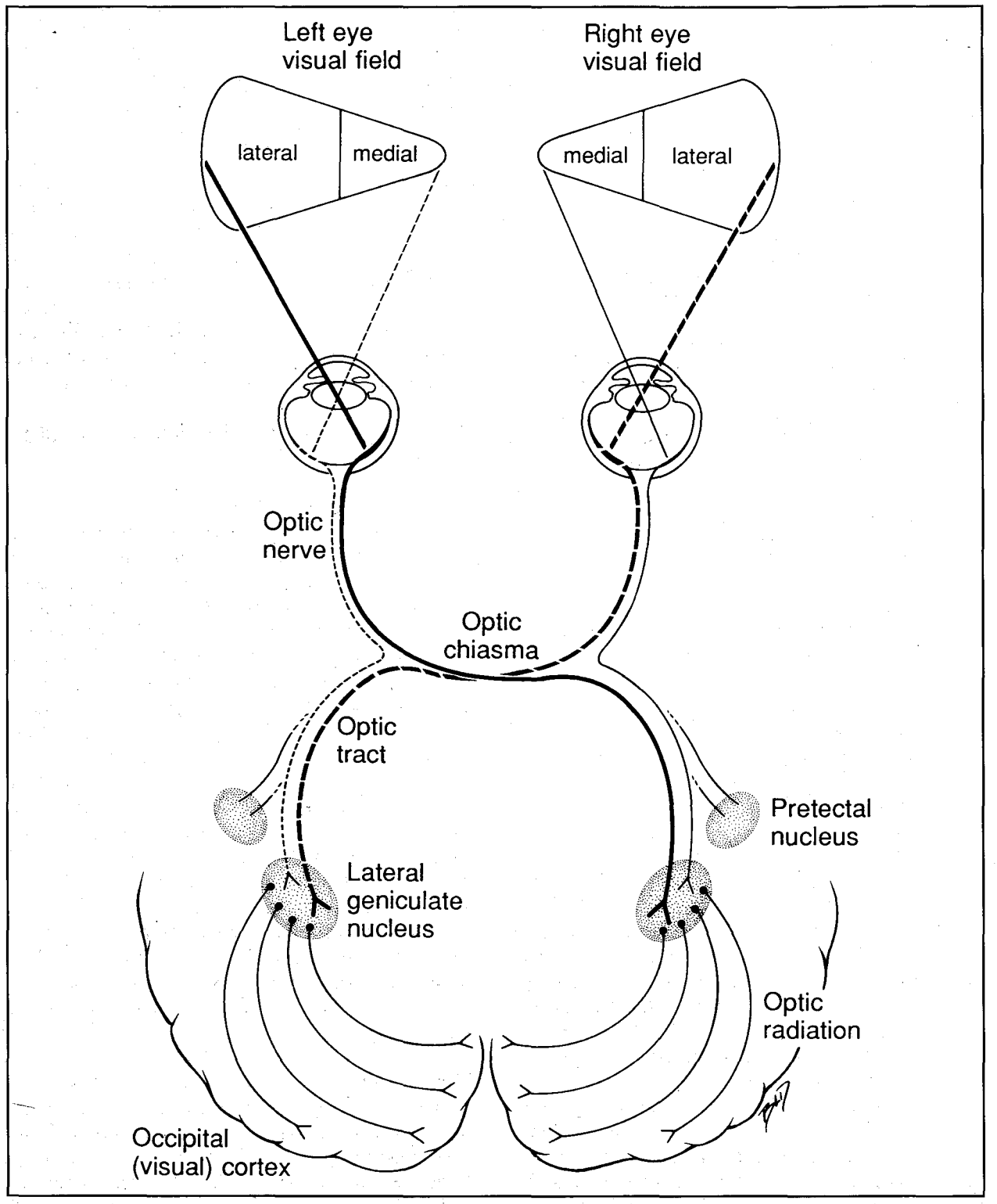

Figure 9.9: Schematic representation of the central visual pathways.

Loss of Vision due to Ophthalmoscopically Detectable Disorders

Optic nerve head abnormalities

A diagram of the retina is shown in Figure 9.10. The axons of the ganglion cells within the inner retina come together to penetrate the sclera at the lamina cribrosa, forming the optic nerve. At the level of the head of the optic nerve (optic nerve head, optic disc), the previously nonmyelinated axons gain a myelin sheath, giving the optic disc a whitish colour.

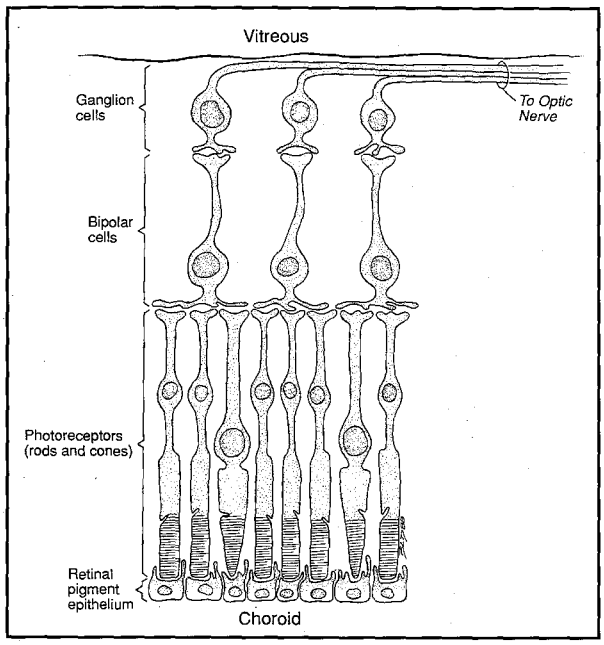

Figure 9.10: Diagram to show the relationships between photoreceptors, bipolar cells and ganglion cells.

Optic nerve hypoplasia may be unilateral or bilateral; it results in visual impairment or blindness. The pupil of the affected eye will either be dilated and non-responsive, or abnormally slow to respond. Ophthalmoscopically, the optic disc will be very small and usually greyish in colour. It has been suggested that this may be an inherited condition in the miniature poodle and it is seen sporadically in other breeds (Kern and Riis 1981).

Papilloedema is a pathological swelling of the optic nerve head. It must be distinguished from "pseudopapilloedema", which is a normal variation and is due to the axons of the ganglion cells gaining a myelin sheath slightly prior to the level of the lamina cribrosa. This gives the disc an irregular and "fluffy" appearance, and is common in some breeds of dog such as the German shepherd dog and Golden retriever. With true papilloedema, the affected optic nerve head appears enlarged and raised, often with engorgement of the superficial blood vessels and oedema of the surrounding retina. Papilloedema may develop in animals with optic nerve tumours and other intracranial neoplasms, and can be a useful indicator of their presence (Palmer *et al* 1974), but is an inconsistent finding. It may also occur as a result of other conditions such as acute pancreatitis (Rubin 1974). Papilloedema itself does not cause visual impairment.

Papillitis is inflammation of the optic nerve head and results in a loss of vision. The optic nerve head is swollen, and may have haemorrhages on its surface. The adjacent retina may also be involved. Canine distemper virus (CDV) infection and granulomatous meningoencephalomyelitis (GME) are possible causes in dogs, but in most patients the aetiology remains obscure. High levels of systemic corticosteroids may suppress the inflammation and restore vision, but relapses are possible.

Optic nerve head atrophy. Permanent damage to the optic nerve or optic tracts results in the dying back of axons to their origin at the ganglion cells, and eventually to the loss of the ganglion cells themselves. The affected optic nerve head appears shrunken and grey. Optic nerve head atrophy takes time to develop and will not be present when the animal first suffers from a loss of vision. It is also a feature of advanced generalised retinal degeneration and glaucoma.

Loss of Vision in Non-Ophthalmoscopically Detectable Diseases

The central visual pathways

Information from the photoreceptors of the outer retina is processed within the inner retina and then conveyed via axons of the ganglion cells, which form the optic nerves. The optic nerves converge at the optic chiasma, where a proportion of axons cross to the contralateral side. The optic tracts are formed by the continuation of the ganglion cell axons. Those fibres involved in the conscious perception of vision synapse in the lateral geniculate nucleus, and the post synaptic fibres form the optic radiation to the visual (occipital) cortex. In general terms, visual information from one side of the body projects to the opposite cerebral cortex, i.e. the image formed on the medial retina of the left eye and the lateral retina of the right eye (images from the left of the body) project to the right cerebral cortex and vice versa. In domestic animals more than half of the optic nerve fibres cross (decussate) at the optic chiasma to the opposite side of the body. In cats 65% of fibres decussate, whereas in dogs 75% of fibres cross over. This is in contrast to man where 50% of the visual fibres decussate.

Neuronal pathway for the pupillary light reflex

Axons from the ganglion cells of the retina that are involved in the PLR accompany those concerned with conscious perception of vision as far as the optic tracts (Figure 9.11). They pass the lateral geniculate nucleus (where fibres of the central visual pathways synapse)

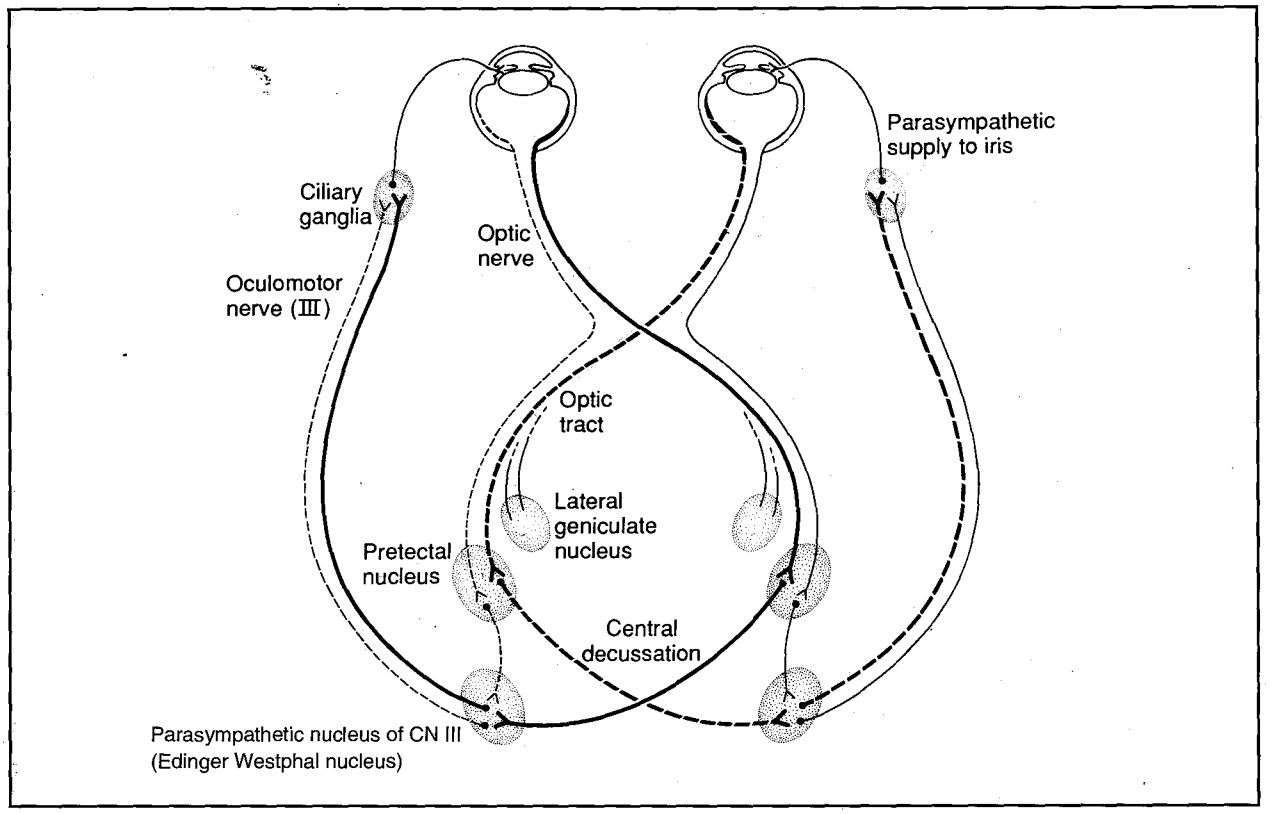

Figure 9.11: Neuronal pathway for pupillary light reflex.

to synapse in the pretectal nucleus. The majority of post synaptic fibres travel to the contralateral parasympathetic nucleus of CN III (the Edinger-Westphal nucleus). Parasympathetic nerve fibres from this nucleus initially pass within the oculomotor nerve, and then on to the ciliary ganglion where they synapse. Post synaptic axons pass via the short ciliary nerves to innervate the pupillary constrictor muscles. This pathway is the efferent arm of the pupillary light reflex. (The sympathetic nervous system innervates the pupillary dilator muscle and plays little part in the PLR). The unequal decussation of fibres concerned with the pupillary light reflex at both the chiasma and also after the pretectal nucleus means that in domestic animals the direct pupillary response is slightly greater than the contralateral response.

Linking the results of the tests for visual deficits with those for PLRs

Localisation of lesions involving the central visual pathways is possible by careful vision testing and assessment of the pupillary light response. Figure 9.12 shows the effect of lesions on the visual fields and Figure 9.13 is a flow diagram to help link the results of vision testing with the PLRs. The central visual pathways may be divided into four regions:

- prechiasmal section (retina and optic nerves)
- optic chiasma
- optic tracts (pre-lateral geniculate nucleus)
- lateral geniculate nucleus, optic radiation and visual cortex.

Prechiasmal lesions (retina or prechiasmal optic nerve)

- **Vision:** affected eye is visually impaired or blind (owners may not notice unilateral vision loss).
- **Changes in PLR:** bilateral lesions result in fixed, dilated, relatively non-responsive pupils (note, some pupillary constriction may occur in animals blind because of severe retinal disease, as less light is required to drive the PLR than is required for vision). Unilateral lesions cause a static anisocoria (pupil on the affected side is more dilated), but the pupils dilate evenly in darkness. The direct PLR and the consensual PLR from the affected eye is absent. With the swinging flashlight test, when the light is moved from the normal to the abnormal eye both pupils dilate. The cover test is "positive" (abnormal) - when the unaffected eye is covered the pupil on the affected side dilates.
- **Further investigations:** careful observation to detect exophthalmos caused by orbital space-occupying lesions; fundoscopy; electroretinography to distinguish between retinal and optic nerve lesions; brain imaging.
- **Aetiology:** optic nerve hypoplasia is one possible cause that can be detected ophthalmoscopically (see above). Sudden onset blindness may result from optic neuritis (Fischer and Jones 1972) or sudden acquired retinal degeneration syndrome (SARD) (van der Woerdt *et al* 1991).

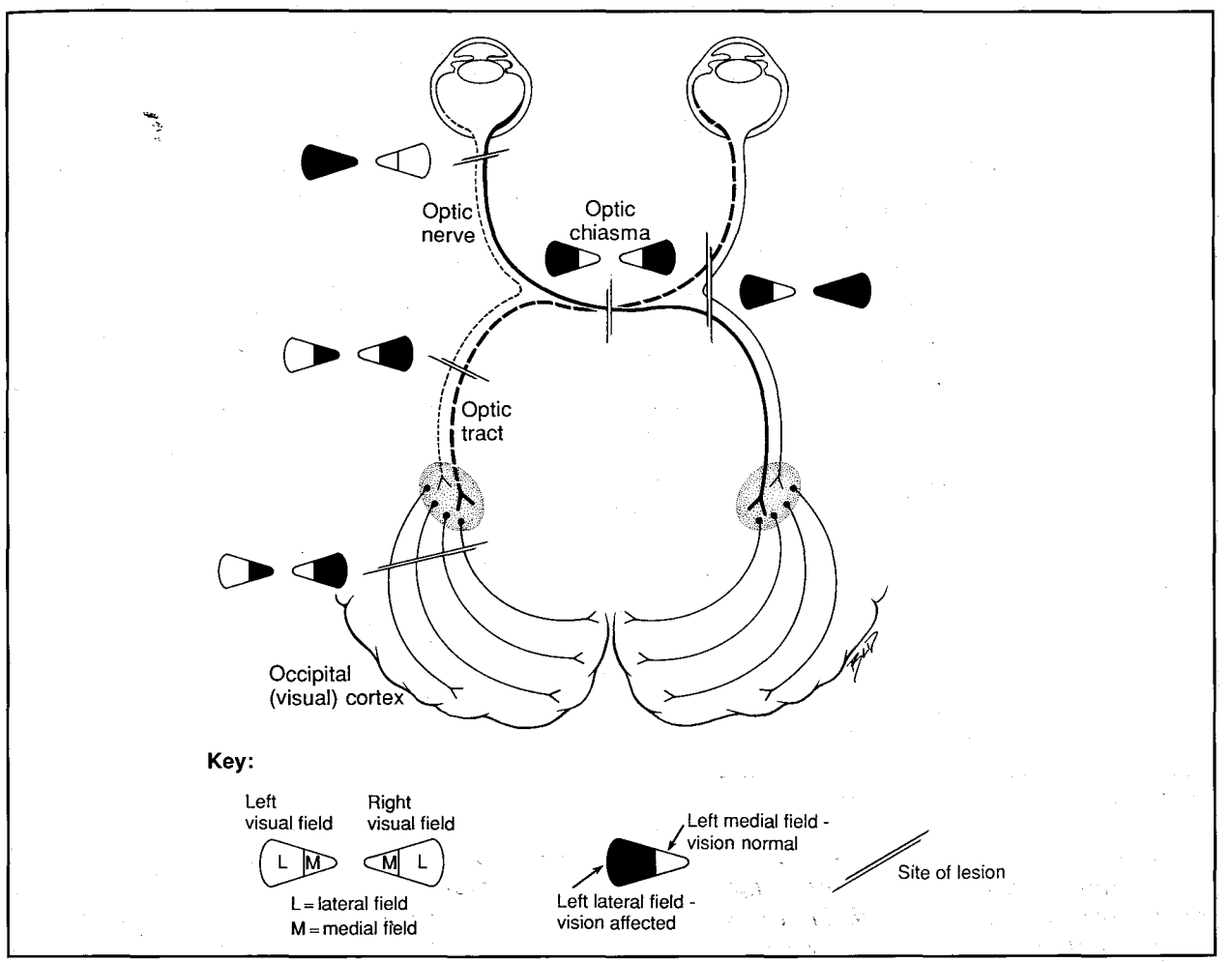

Figure 9.12: Effect on visual fields of lesions within the central visual pathways at various levels.

If papillitis is present in animals suffering from optic neuritis, the diagnosis can be made ophthalmoscopically. However, if just the retrobulbar portion of the nerve is affected, there may be no ophthalmoscopically detectable signs. Similarly, with SARD initially there are no detectable fundus changes and yet the affected animal is blind. Electroretinography is required to distinguish between optic neuritis and SARD; the electroretinogram is unaltered in optic neuritis, but is extinguished in SARD. This differentiation is important because optic neuritis may respond to systemic corticosteroids, but SARD will not. Other causes include neoplasia (Williams *et al* 1961; Barnett *et al* 1967), trauma and optic nerve compression.

Lesions of optic chiasma

- **Vision:** affected in both eyes.
- **Changes in PLR:** complete lesions cause dilated, unresponsive pupils.
- **Further investigations:** brain imaging.
- **Aetiology:** neoplasia (Braund *et al* 1977; Skerritt *et al* 1986). Other causes include vascular occlusions and inflammatory processes.

Optic tract lesions, prior to divergence of fibres of PLR

- **Vision:** unilateral lesions result in the loss of the medial visual field of one eye and the lateral visual field of the other eye (homonymous hemianopia). The vision of the eye contralateral to the optic tract lesion will be most affected.
- **Changes in PLR:** with unilateral lesions the pupil on the contralateral side to the lesion will remain more dilated during the swinging flashlight and cover tests. Both pupils dilate normally in darkness.
- **Further investigations:** check for other neurological deficits such as a hemiparesis and hemisensory defect of the side of the body contralateral to the lesion; brain imaging.
- **Aetiology:** unilateral lesions may be caused by space-occupying lesions (deLahunta and Cummings 1967) or inflammatory lesions. Ischaemia following a vascular occlusion is another possible cause, but is rare in dogs. Inflammation of both optic tracts may result from CDV infection.

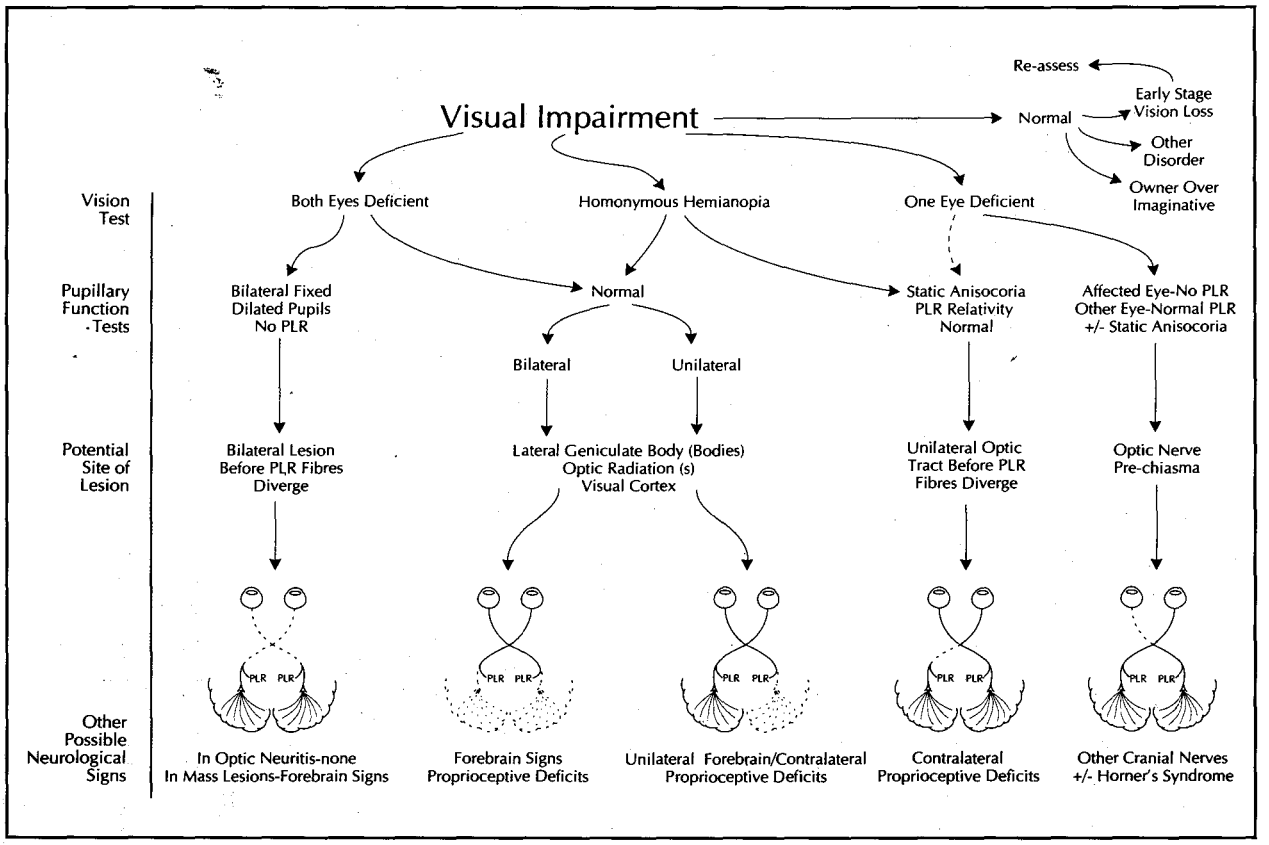

Figure 9.13: Flow diagram to help link the results of vision testing with those of pupillary light reflex testing. (The broken lines on the visual pathway indicate the site of the lesion).

Lesions affecting the lateral geniculate nucleus, optic radiation or occipital cortex

- **Vision:** as for optic tract lesions (see above).
- **Changes in PLR:** pupillary responses are normal.
- **Further investigations:** check for other neurological deficits such as a hemiparesis and hemisensory defect of the side of the body contralateral to the lesion; brain imaging.
- **Aetiology:** unilateral lesions may result from neoplasia, inflammation or trauma. Encephalitis and vascular occlusions are additional causes. Bilateral visual defects, along with other severe neurological abnormalities, are seen in many disease processes affecting the forebrain, particularly trauma, space-occupying lesions, and encephalitis.

SECTION II DIFFERENCES IN PUPIL SIZE - ANISOCORIA

Anisocoria is a difference in size of pupils, which may result from intraocular disease (e.g. glaucoma, uveitis, synechiae) or from interference with the parasympathetic (part of PLR arc) or sympathetic nerve supply to the iris musculature.

Lesions within the Afferent Pathway of the Pupillary Light Reflex

Afferent nerve fibres involved in the PLR diverge from fibres concerned with vision just before the lateral geniculate nucleus. Lesions affecting the fibres prior to that point also affect vision and are considered above. The fibres concerned with PLRs may be damaged as they pass between the optic tracts and the oculomotor nuclei. Lesions at these sites spare vision. The effect on the pupillary responses of lesions prior to the central decussation is the same as caused by lesions of the ipsilateral optic tract prior to the lateral geniculate nucleus.

Lesions within the Efferent Pathway for Control of Pupillary Size

Lesions of the oculomotor nerve will affect the parasympathetic nerve supply to the pupillary sphincter muscle. Total lesions result in a dilated unresponsive pupil. The oculomotor supply to the extraocular muscles may also be affected; ptosis and a ventrolateral strabismus result.

Feline dysautonomia may affect the para-sympathetic control of the pupils resulting in fixed, dilated pupils (Chapter 12).

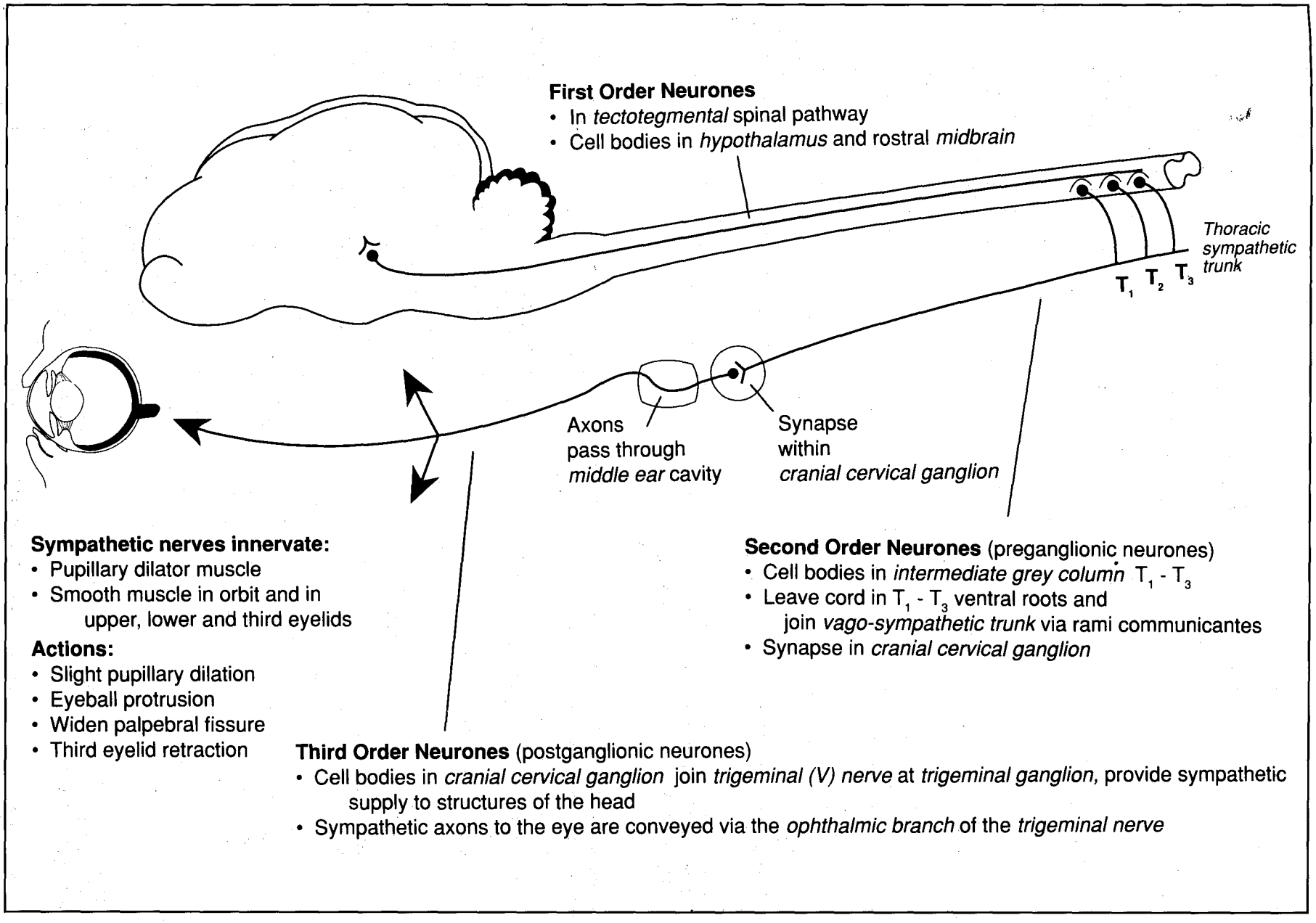

Figure 9.14: *Sympathetic nerve supply to eye and adnexa.*

Pharmacological testing

Pharmacological testing may help to localise the site of the lesions within the PLR arc.

a. **Direct acting parasympathomimetic** (e.g. Pilocarpine 1% drops). Topically administered pilocarpine can be used to differentiate between UMN (i.e. pretectal nucleus to oculomotor nucleus) and LMN lesions. LMN lesions result in hypersensitivity to pilocarpine, the iris circular muscle fibres contracting more rapidly than normal. UMN lesions do not result in this hypersensitivity.

b. **Indirect acting parasympathomimetics** (e.g. 0.5.% physostigmine drops) cause no pupillary change with postganglionic lesions. (The ganglion referred to is the ciliary ganglion). There is rapid pupillary constriction when either preganglionic lesions or UMN lesions are present. The pupil of the normal eye constricts within 40-60 minutes.

Sympathetic Innervation of the Eye

The sympathetic nervous system innervates the pupillary dilator muscles, and sympathetic denervation results in a miotic (constricted) pupil. This occurs as part of Horner's syndrome.

The sympathetic nervous system supply to the eye is shown in Figure 9.14 (Barlow and Root 1949). Smooth muscle within the orbit, upper, lower and third eyelids is also innervated by the sympathetic nervous system. This keeps the eyeball protruded, the palpebral fissure widened and the third eyelid retracted. The sympathetic innervation of the iris results in some dilation of the pupil, which is increased by excitement, stress etc. Note that reduced tone in the pupillary constrictor muscle (parasympathetic supply) is responsible for pupillary dilation in reduced light.

Horner's syndrome

Interference with the sympathetic nerve supply to the head results in a combination of signs, collectively referred to as Horner's Syndrome.

- **Miosis:** the pupil on the affected side is smaller than the unaffected pupil
- **Protrusion of the membrana nictitans (third eyelid):** due to lack of tone in the smooth muscle retracting it, and also secondary to enophthalmos
- **Upper eyelid ptosis (incomplete elevation):** due to reduced tone in Muller's muscle; laxity of the lower eyelid may also be observed, particularly in dogs; in cats the palpebral fissure appears narrowed
- **Enophthalmos:** resulting from a lack of tone in the orbital smooth muscle allowing the eye to sink back into the orbit
- **Other changes:** these include a slight reduction in intraocular pressure, and peripheral vasodilation resulting in a warmer pinna, and a slight engorgement of conjunctival blood vessels.

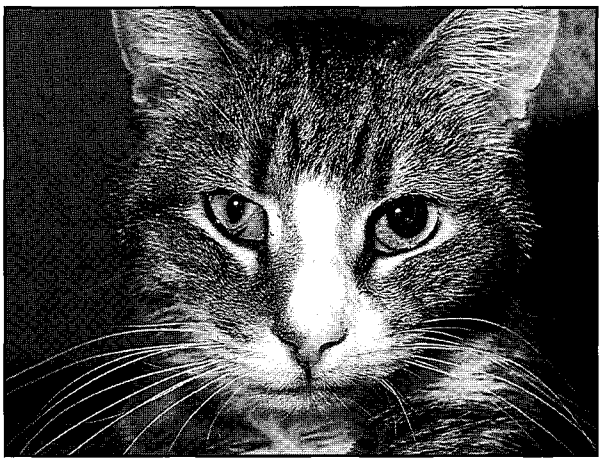

Figure 9.15: Cat with Horner's syndrome. Note ptosis (narrowed palpebral fissure), third eyelid protrusion and miosis in affected eye

Horner's syndrome may result from lesions of the sympathetic supply to the head at any one of three anatomical levels, resulting in a first, second or third order Horner's syndrome (Figure 9.16). Other clinical signs and pharmacological differentiation may aid in localising the lesion.

Pharmacological differentiation (Bistner *et al* 1970). 10% phenylephrine is administered topically to both eyes, and the time taken to dilate the pupils is noted. The results are as follows:

- **Normal eye and first order Horner's syndrome:** pupil dilates in 60-90 minutes
- **Second order Horner's syndrome:** pupil dilates in about 45 minutes
- **Third order Horner's syndrome:** pupil dilates in about 20 minutes

The increased sensitivity to phenylephrine in second and third order Horner's syndrome is due to denervation hypersensitivity. In addition to dilating the pupil, other local signs of Horner's syndrome are abolished by topical phenylephrine.

Other investigations. Full neurological examination. Radiographs of the cranial thorax, cervicothoracic spine and middle ear may help localise the lesion, though in many cases the aetiology remains obscure. Golden retrievers in the UK are relatively commonly affected with an apparently idiopathic Horner's syndrome.

Anisocoria Following Intracranial Trauma

Intracranial trauma may result in abnormalities in pupil size. Forebrain lesions, with subsequent brain swelling and herniation, initially result in sluggish PLRs. Later, as the problem progresses, the pupils become fixed dilated, because of compression of the oculomotor nerve or midbrain. In animals where brain swelling is suspected (e.g. following trauma, or where there is encephalitis or neoplasia) it is usual to monitor the PLR regularly. This type of pupillary change can be unilateral, and may be ipsilateral or contralateral to the lesion.

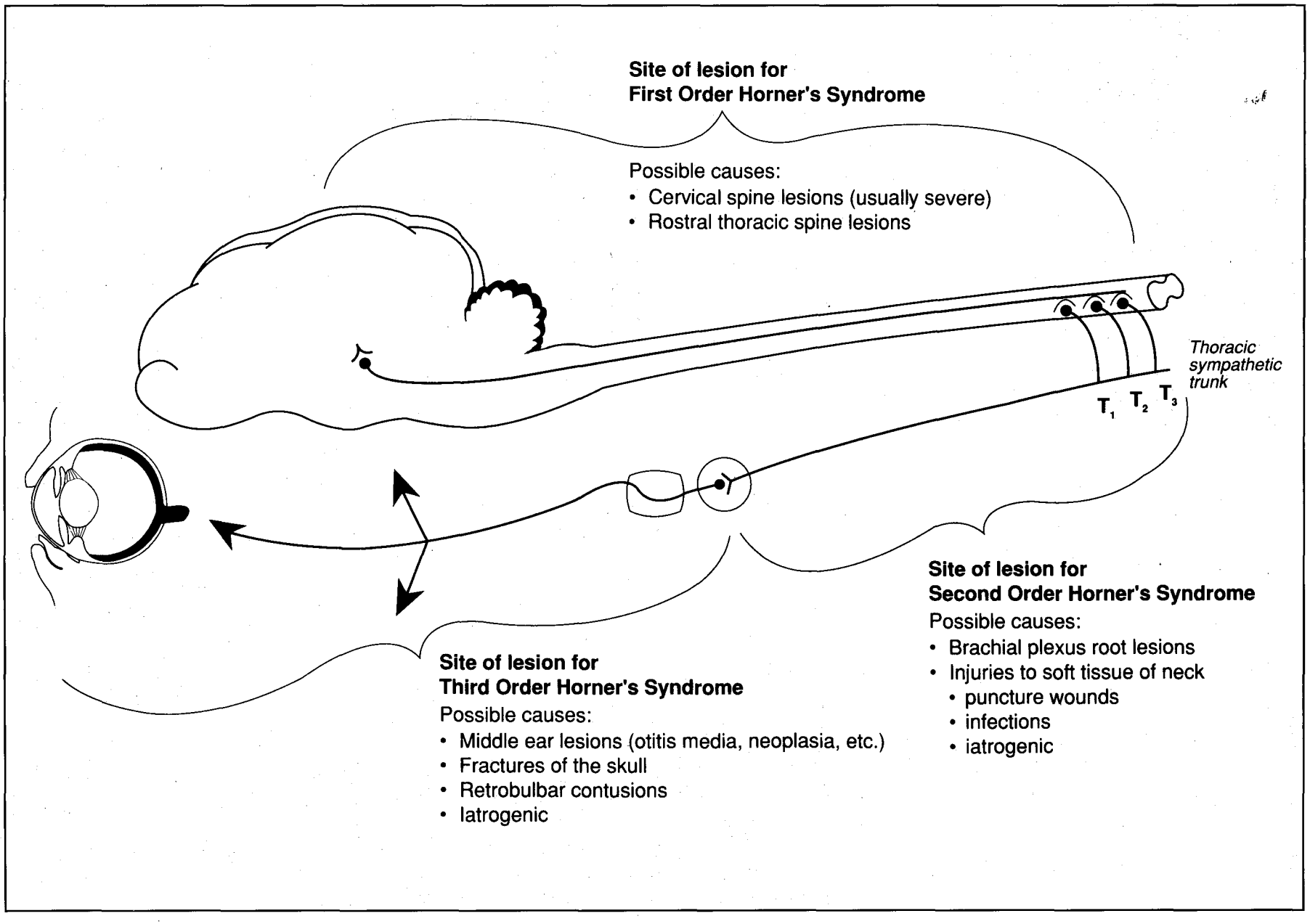

Figure 9.16: *Sites of lesions resulting in Horner's syndrome and possible aetiologies.*

SECTION III
DISORDERS AFFECTING EYE POSITION AND MOVEMENT

Strabismus - Abnormalities of Eye Position

Nerve supply to the extraocular muscles (Figure 9.17).

- **Oculomotor (III) nerve** innervates dorsal, medial and ventral rectus muscles, the ventral oblique muscle and the levator palpebrae superioris. Parasympathetic fibres, which travel within the nerve, supply intraocular smooth muscle. Interference with the parasympathetic component of the oculomotor nerve results in a fixed, dilated pupil. When the general somatic efferent component of the nerve is affected there is a lateral and ventral strabismus (the "down and out eye") and an upper lid ptosis (drooping).
- **Trochlear (IV) nerve** innervates the dorsal oblique muscle. Lesions result in rotation of the globe with the dorsal portion turned laterally (most readily detected in cats because of their pupil shape).
- **Abducens (VI) nerve** innervates the lateral rectus and retractor bulbi muscles. Lesions of the abducens nerve result in a medially diverted globe (esotropia) which cannot be abducted.

Squints or strabismus

These are seen relatively commonly, and may occur congenitally, or as a result of lesions of the extraocular muscles or their nerve supply.

Congenital strabismus may be seen in any breed of dog or cat. A common example is the bilateral convergent strabismus (esotropia) of some Siamese cats.

Traumatic proptosis of the globe may cause tearing of the rectus muscles (usually the medial rectus muscle). If the globe is subsequently saved, a strabismus will remain. A divergent strabismus or exotropia results from tearing of the medial rectus muscle.

Retrobulbar swelling (due to infection or neoplasia) may cause strabismus in addition to exophthalmos.

A ventrolateral strabismus is often a feature of vestibular disease, and is most obvious when the head is elevated.

Disorders of Eye Movements (Abnormal Nystagmus)

The co-ordination of eye movements is a complex mechanism with inputs from the vestibular systems, cerebellum and higher centres. Communication between the nuclei of the nerves to the extraocular

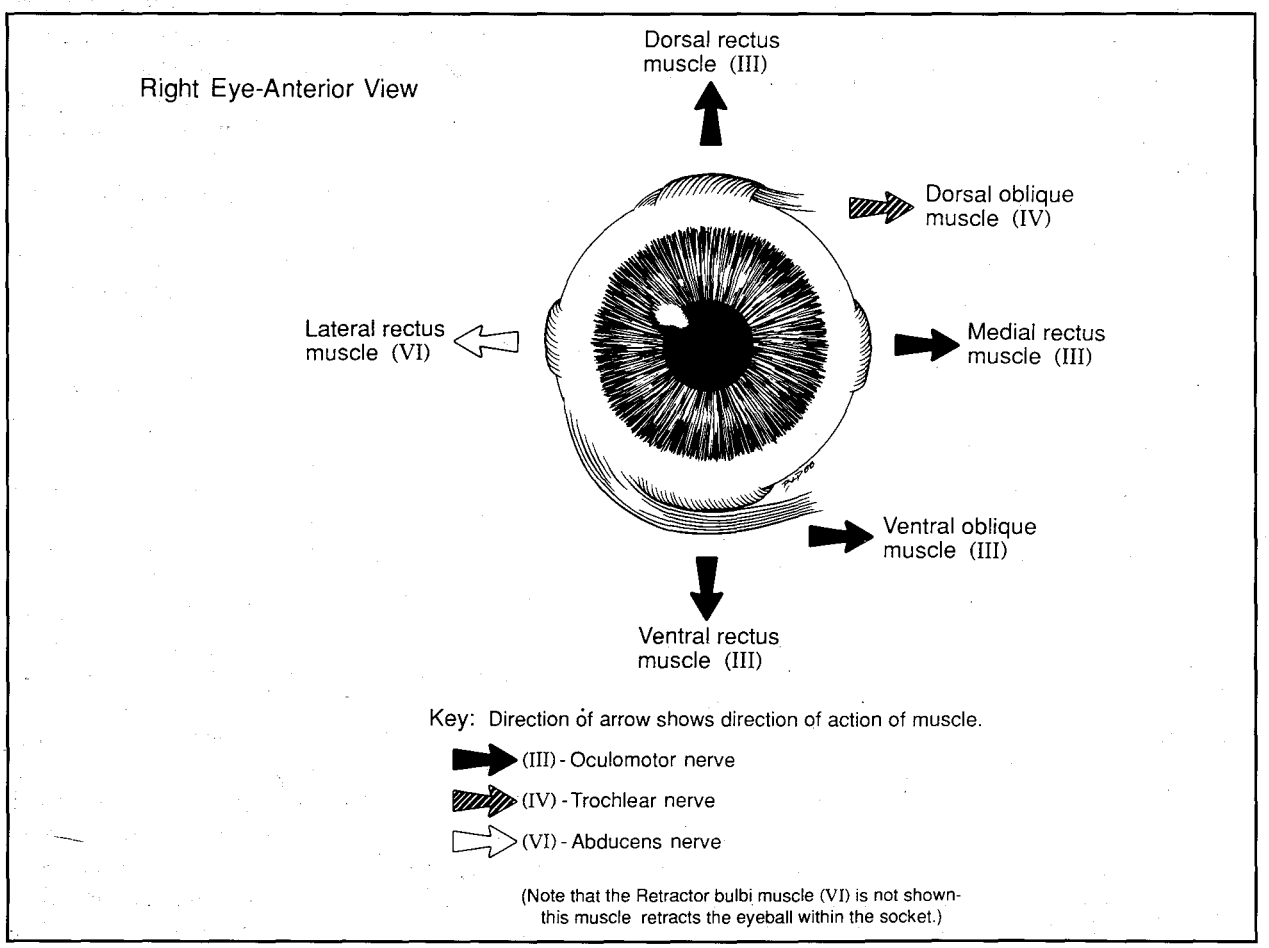

Figure 9.17: Diagram showing the extraocular muscles, their actions and innervation.

muscles occurs via the medial longitudinal fasciculus and helps co-ordinate the extraocular muscles.

Disorders of eye movement can be observed during the oculocephalic reflex (see Part 1 of this chapter).

Vestibular influence on eye movements

The vestibular system is involved in controlling the animal's eye movements and position, as well as maintaining the position of the trunk and limbs in relation to the head. It is also involved in normal nystagmus, as induced by the oculocephalic reflex (see Part 1 of this chapter).

Abnormal nystagmus

This may occur as a congenital disorder, or as an acquired condition in vestibular or cerebellar disease. When abnormal nystagmus occurs in an unrestrained animal it is known as "spontaneous nystagmus". If it can be induced, or the direction changes by holding the head in an abnormal position, it is called "positional nystagmus". The latter is often a feature of central vestibular disease.

- **Congenital nystagmus** occurs most commonly in puppies with microphthalmos and associated intraocular disorders such as persistent pupillary membranes and cataract. It appears as continual fine oscillations of the globes, often in a rotary fashion. Congenital nystagmus is sometimes observed in puppies or kittens with no other detectable abnormalities. Congenital blindness may be accompanied by continuous, almost random eye movements described as a "searching nystagmus".
- **Nystagmus due to peripheral vestibular disease** is a spontaneous horizontal (or sometimes rotary) nystagmus. The direction of the nystagmus (i.e. the fast phase) is away from the side of the lesion and remains the same whatever the head position. Other signs of vestibular disease such as head tilt, circling, loss of balance, etc. will also be present.
- **Nystagmus due to central vestibular disease** may be a horizontal, vertical or positional nystagmus (where the direction of nystagmus changes as the position of the head is altered). Other neurological signs typical of vestibular disorders will be present.
- **Nystagmus due to cerebellar disorders** is a form of intention tremor of the extraocular muscles.

SECTION IV
ABNORMALITIES OF BLINK

Normal blinking is important for maintaining a healthy ocular surface. A deficiency of blink results in varying degrees of corneal disease. Lack of a normal blink may result from lesions of the afferent (sensory) or efferent (motor) arms of the blink reflex.

Abnormalities of Blink due to Sensory Deficit

Sensory innervation of the eye

Sensory innervation of the globe and adnexa is via the trigeminal (V) nerve as follows:

- **Ophthalmic branch:** globe and middle portion of the upper eyelid
- **Maxillary branch:** lateral portion of the upper eyelid, the lower eyelid and surrounding skin

The trigeminal nerve transmits sensory impulses to the trigeminal nucleus in the brain stem. After synapsing, these impulses cross to the contralateral thalamic nuclei and from there to the cerebral cortex for conscious perception. The corneal reflex is used to assess corneal sensation; the efferent arm of this reflex is via the facial (VII) nerve.

Sensory denervation of the globe

- **Signs:** a neurotrophic keratitis results from a sensory deficit of the cornea. Ulceration usually affects most of the cornea within the interpalpebral fissure. Note that the menace response will still cause the animal to blink if the eye is still visual. Infranuclear lesions (i.e. those occurring between the sensory nerve endings and the cells of the trigeminal nuclei) may result in total anaesthesia or partial anaesthesia. Hypalgesia of the three branches of the trigeminal nerve due to a supranuclear lesion is quite common. Often a supranuclear facial nerve palsy is present as well, because of the close proximity of thalamic nuclei (V) and the internal capsule (VII).
- **Aetiology:** neoplasia, infection or skull fractures, and polyneuropathy.
- **Treatment:** identify the site and cause of the lesion and treat if possible. Treat neurotrophic keratitis with covering topical antibiotics and tear substitutes.

Abnormalities of Blink due to Motor Defects

Motor innervation of eyelids

The facial (VII) nerve supplies the muscles of facial expression, and carries parasympathetic nerves innervating the lacrimal glands. It passes from the brain alongside the auditory nerve until it enters the facial canal, which passes adjacent to the medial wall of the tympanic cavity. Fibres innervating the lacrimal gland pass via the major petrosal nerve and are given off just as the facial canal bends to become adjacent to the tympanic cavity. This close anatomical association between the facial nerve and the tympanic cavity is of clinical significance. The facial nerve emerges through the stylomastoid foramen and innervates the muscles of facial expression including the orbicularis oculi muscle, which is responsible for blinking. The ability to blink may be checked by a number of tests, such as the menace response and corneal reflex.

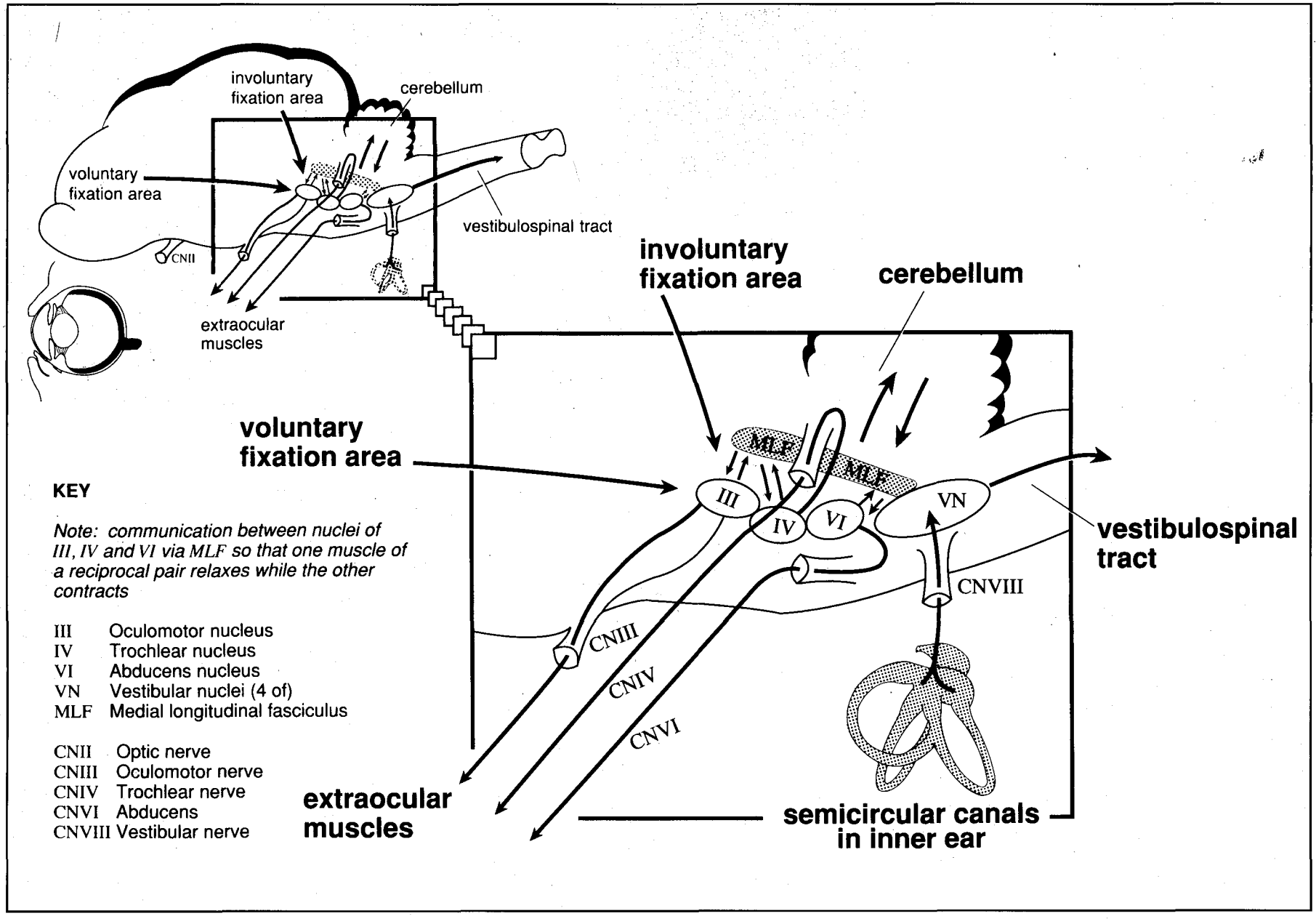

Figure 9.18: Diagram to show the pathway for vestibular influence of eye movements.

Lesions of the facial nerve

- **Signs:** facial nerve paralysis results in an inability to blink, and weakness of the facial muscles. When the animal is stimulated to attempt to blink by the menace test or corneal reflex, the globe is retracted and the third eyelid flicks across the cornea, but the upper and lower lids are incapable of closing the palpebral fissure. The cornea will be unaffected in cases where the parasympathetic supply to the lacrimal gland is spared, if the third eyelid can adequately distribute the tear film.
- **Aetiology:** neoplasia, infection or skull fractures are possible causes. A number of cases are idiopathic, and some patients with facial paralysis are suffering from polyneuropathy (Chapter 14). Facial paralysis is commonly seen in otitis media / interna.
- **Treatment:** identify the cause and treat if possible. Ocular treatment is not usually necessary unless lacrimal function is impaired, or the affected animal is brachycephalic and thus movement of the third eyelid across the globe cannot spread the tear film adequately, in which case tear substitutes should be used.

Hemifacial spasm. This is the result of increased motor activity of the facial nerve. It may, at first glance, be confused with facial nerve paralysis of the contralateral side. It has been reported in dogs with chronic otitis media (irritation of facial nerve) and following facial paralysis; central causes have also been suggested (Parker *et al* 1973; Roberts and Vainisi 1967).

SECTION V
DISORDERS OF LACRIMATION

The afferent arm for the tearing reflex is via the trigeminal nerve. The efferent arm takes the following route. Preganglionic axons leave the brain stem within the facial nerve and pass via the major petrosal nerve. This nerve diverges from the facial nerve within the facial canal in the medial wall of the middle ear cavity, and passes through the pterygoid canal to end in the pterygopalatine ganglion. Post ganglionic fibres take this route to innervate the lacrimal glands.

Tear production may be measured by the **Schirmer tear test.** A specially shaped strip of filter paper is hooked between the lower lid and cornea, and left in situ for one minute (Figure 9.19). The length of strip which is wet with tears after this time is measured. The normal reading is about 15-25 mm/minute.

Lesion of the afferent arm of the tearing reflex

Sensation conveyed from the cornea, conjunctiva and to a certain extent the nasal mucosa via the trigeminal nerve acts as the afferent arm of the reflex to increase tear production. Lesions of the trigeminal nerve have been discussed above.

Lesions of the efferent arm of the tearing reflex

Lesions affecting the parasympathetic supply to the lacrimal gland may also involve the facial nerve. There is a much reduced tear production leading to corneal desiccation and possibly corneal perforation. Lesions may occur secondary to severe otitis media or middle ear neoplasia.

Non-neurological causes of dry eye (keratoconjunctivitis sicca) are much commoner than neurological causes, especially in dogs.

The cause of dry eye should be identified and treated, if possible. Topical tear substitutes and ointments can be used and oral parasympathomimetics such as pilocarpine may be of benefit in neurogenic cases. A parotid duct transposition may be performed if medical treatment fails to control the condition.

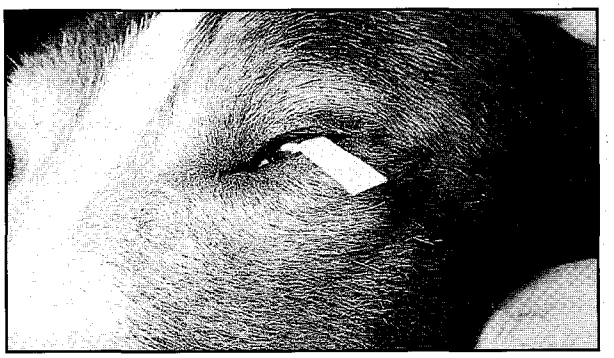

Figure 9.19: *Performing a Schirmer tear test.*

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CHAPTER TEN

Neurological Deficits in Multiple Limbs: Spinal disorders

Simon J. Wheeler and Nicholas J. H. Sharp

INTRODUCTION

The identification of neurological deficits in multiple limbs should allow the clinician to localise the lesion to an area of the nervous system using the information given in Part 1 of this manual.

In some patients, the origin of the locomotor disturbance may not be in the nervous system. Thus, prior to the neurological examination, a careful physical examination must be performed. Some examples of conditions that may mimic neurological presentations are given in Table 10.1.

Table 10.1: Conditions mimiking spinal presentations

Bilateral orthopaedic conditions
Limb / pelvic fractures
Osteochondritis dissecans
Cranial cruciate ligament rupture
Tibial crest avulsion
Generalised conditions
Panosteitis
Polyarthritis
Hypertrophic osteodystrophy
Soft tissue disorders
Infraspinatus muscle contracture
Gracilis muscle contracture
Quadriceps muscle contracture
Vascular disease

Neurological deficits in the limbs generally occur caudal to a lesion. Thus, deficits in the pelvic limbs may indicate disease in any part of the nervous system. If there are thoracic limb deficits, a solitary lesion will be cranial to the thoracic spinal cord segments. Of course, it is always possible that there are multiple lesions.

Lesions affecting multiple limbs may originate in one of three sites: intracranial, spine or peripheral neuromuscular system. This chapter considers spinal diseases. The other categories are dealt with elsewhere in this book. The neurological examination should indicate which of the sites is affected.

Once the lesion has been localised to an area of the spinal cord, a list of differential diagnoses can be drawn up. Examples are given in Table 10.2.

It should also be noted that many of the conditions described have the **potential** to cause the type of neurological signs described. In many of the conditions, pain or spinal hyperaesthesia are frequently seen. In fact, this may be the only clinical sign at certain stages of the disease. The presence of pain is useful in lesion localisation, whether or not neurological deficits are present.

Once a list of differential diagnosis has been drawn up, the diagnosis can be confirmed by use of the ancillary diagnostic tests described in Part 1. In most patients with spinal disease the following will be the most useful diagnostic tests: survey radiography, CSF analysis, and myelography. If facilities are limited and all these modalities are not available, the clinician should think carefully before embarking of a course of action that may provide only part of the information. For example, it is probably redundant to perform survey radiographs on a Dobermann where the "Wobbler's syndrome" is suspected, as full evaluation requires myelography. If the primary clinician is unable to perform a myelogram, it is probably better to refer the patient without taking survey radiographs. However, if the patient is to be referred, it is useful for the primary clinician to perform basic blood work (haematology and biochemistry), as most referral clinicians will require this information as a precursor to diagnostic procedures and surgery.

Table 10.2: Important spinal diseases by area of spinal cord

IMPORTANT SPINAL DISEASES BY AREA OF SPINAL CORD

(The most likely diagnoses in immature animals are indicated *.)

Modified from *Small Animal Spinal Disorders: Diagnosis and Surgery.* SJ Wheeler and NJH Sharp. Wolfe-Mosby, London.

C_1-C_5

Acute

Painful
- Disc disease
- Atlantoaxial subluxation*
- Caudal cervical spondylomyelopathy
- Neoplasia
- Inflammatory CNS disease*
- Discospondylitis*
- Trauma*

Non-Painful
- Ischaemic myelopathy

Chronic

Painful
- Disc disease
- Atlantoaxial subluxation*
- Caudal cervical spondylomyelopathy
- Neoplasia
- Inflammatory CNS disease*
- Discospondylitis*

Non-Painful
- Storage diseases*
- Congenital vertebral malformations
- Syringomyelia
- Neoplasia

C_6-T_2

Acute

Painful
- Disc disease
- Caudal cervical spondylomyelopathy
- Neoplasia
- Inflammatory CNS disease*
- Discospondylitis*
- Trauma*

Non-Painful
- Ischaemic myelopathy

Chronic

Painful
- Disc disease
- Caudal cervical spondylomyelopathy
- Neoplasia
- Inflammatory CNS disease*
- Discospondylitis*

Non-Painful
- Congenital vertebral malformations
- Neoplasia

T_3-L_3

Acute

Painful
- Disc disease
- Neoplasia
- Inflammatory CNS disease*
- Discospondylitis*
- Trauma*

Non-Painful
- Ischaemic myelopathy

Chronic

Painful
- Disc disease
- Neoplasia
- Inflammatory CNS disease*
- Discospondylitis*

Non-Painful
- Degenerative myelopathy
- Hereditary myelopathy*
- Spinal dysraphism*
- Syringomyelia
- Congenital vertebral malformations*
- Neoplasia

L_4-S_3

Acute

Painful
- Disc disease
- Neoplasia
- Inflammatory CNS disease*
- Discospondylitis*
- Trauma*
- Sacrocaudal injuries

Non-Painful
- Ischaemic myelopathy

Chronic

Painful
- Disc disease
- Lumbosacral disease
- Neoplasia
- Inflammatory CNS disease*
- Discospondylitis*

Non-Painful
- Spinal dysraphism*
- Spina bifida*
- Sacrocaudal dysgenesis
- Syringomyelia
- Congenital vertebral malformations*
- Neoplasia

Thus, the stages in working up a patient with spinal disease are:

History
Physical examination
Neurological examination
↓
Determine if lesion is neurological
↓
Localise lesion
↓
Draw up differential diagnosis list
↓
Perform diagnostic tests (or refer)
↓
Determine best treatment
↓
Give prognosis

SPINAL DISEASES

The following is a description of the most important spinal diseases in dogs. The diseases are listed alphabetically. For further discussion of feline spinal diseases, see Chapter 15. Key references are given, but the list is not intended to be encyclopaedic. For a fuller listing, see Braund (1986) and LeCouteur and Child (1989). Surgical treatment is indicated in many spinal disorders - see Wheeler and Sharp (1994).

Arachnoid Cysts

In arachnoid cysts there is a focal accumulation of CSF in the subarachnoid space, which compresses the spinal cord (Dyce *et al* 1991). The condition should be suspected in a young dog with progressive signs of myelopathy, but which is pain free. Diagnosis is by myelography. Surgical decompression may be effective.

Atlantoaxial Subluxation

Atlantoaxial subluxation causes pain and neurological deficits, related to cervical spinal cord compression, which range from mild ataxia and proprioceptive deficits to severe tetraparesis (Geary, Oliver and Hoerlein 1967). Neck pain is seen in most patients and can be severe, particularly following trauma. In mild cases, conscious proprioceptive deficits alone may be seen. Weakness or severe paresis indicate more significant spinal cord compression. Asymmetry of signs, or preferential involvement of either the thoracic limbs or pelvic limbs may occur. Tetraplegia is rarely encountered, as spinal cord damage of this severity usually leads to respiratory failure.

The atlantoaxial joint allows rotation of the head. C_1 pivots around the dens of C_2, but there is little flexion possible at this joint. The relationship between C_1 and C_2 is largely maintained by ligaments. There are a number of pathological processes that may lead to atlantoaxial subluxation:

- ***Congenital absence or hypoplasia of the dens*** is the most common. It is most often encountered in small breeds of dog, particularly Yorkshire terriers, Miniature poodles, Pomeranians and Pekinese. Clinical signs are usually seen in immature patients.
- ***Fracture or separation of the dens*** can occur in any type of dog.
- ***Rupture or absence of the ligaments***, particularly the transverse ligament of the atlas and the dorsal atlantoaxial ligament can lead to subluxation.

Diagnosis

Survey radiography provides the diagnosis in most cases (Figure 10.1). General anaesthesia is required for

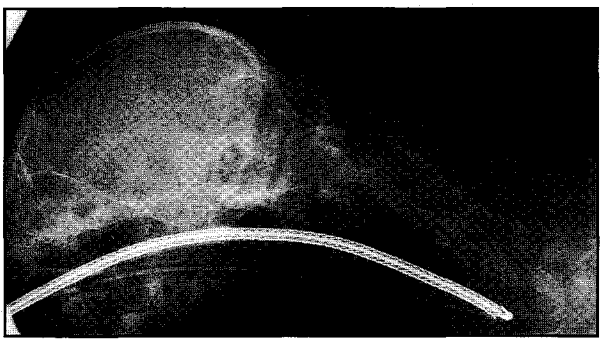

Figure 10.1: *Lateral radiograph demonstrating atlantoaxial subluxation in a Chihuahua.*

taking the radiographs, as accurate positioning is essential. The lateral projection will reveal the presence of subluxation. Mild flexion of the cranial cervical region may be required to demonstrate the malalignment of the vertebra, but this must not be excessive. The ventrodorsal view will highlight the dens and show whether it is present. Myelography is unlikely to be required.

Treatment

Non-surgical treatment by cage rest, application of a neck brace and use of anti-inflammatory medications may lead to improvement, however this is usually transient.

Surgical treatment is indicated in most patients with congenital lesions. Even dogs with profound neurological deficits are likely to benefit from stabilisation. The technique of ventral fusion by lag screws is recommended (Figure 10.2). The prognosis depends largely on the neurological status at presentation; the more severe the deficits, the less favourable the outlook. Dogs with neck pain and mild deficits have a good prognosis (Thomas *et al* 1992).

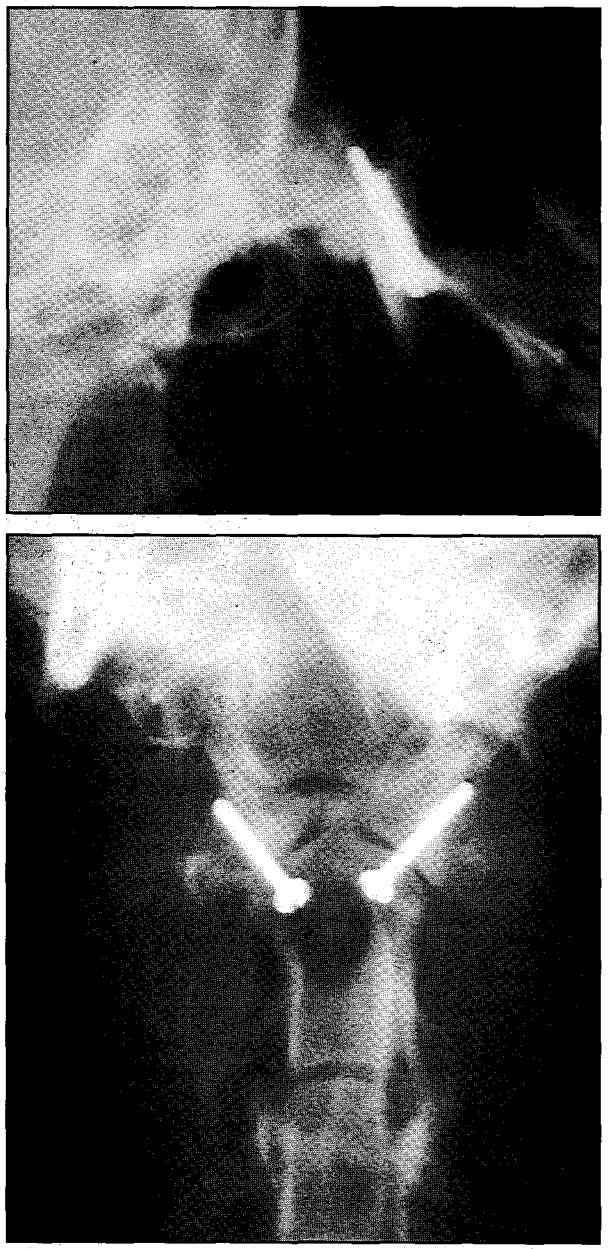

Figure 10.2: ***(a - top)*** *Lateral and* ***(b - bottom)*** *ventrodorsal radiographs: surgical repair of atlantoaxial subluxation with lag screws.*

Caudal Cervical Spondylomyelopathy

Caudal cervical spondylomyelopathy (CCSM) ("Wobbler's syndrome") is a syndrome of large and giant breed dogs, particularly Dobermanns and Great Danes. Signs of ataxia, paresis and cervical pain are caused by spinal lesions, which mainly affect the caudal cervical spine. The cause of this disorder is multifactorial; some of the important contributing factors are:

- Stenosis of the vertebral canal
- Vertebral instability
- Disc herniation
- Ligamentous hypertrophy
- Joint capsule proliferation
- Osteophyte production

(Seim and Withrow 1982).

Clinical signs may be seen in young dogs, particularly Great Danes with severe vertebral canal stenosis. Most other breeds show signs from middle age onwards.

The most common presentation is a gait disturbance most severe in the pelvic limbs. This ranges from mild ataxia and paresis, to marked pelvic limb hypermetria and an associated short-stepping thoracic limb gait. Cervical hyperaesthesia, guarding of the neck, or a low carriage of the head may be seen. Lameness and muscle atrophy in one thoracic limb suggest that nerve root compression is present. Conscious proprioceptive deficits are more pronounced in the pelvic limbs.

Diagnosis

Survey radiographs are useful in ruling out other conditions, but they are not accurate in locating the site of cord compression (Seim and Withrow 1982). They must always be taken under general anaesthesia. Stressed views are not useful in survey radiography.

Myelography is the most important diagnostic aid, and both lateral and ventrodorsal projections should be taken (Figure 10.3).

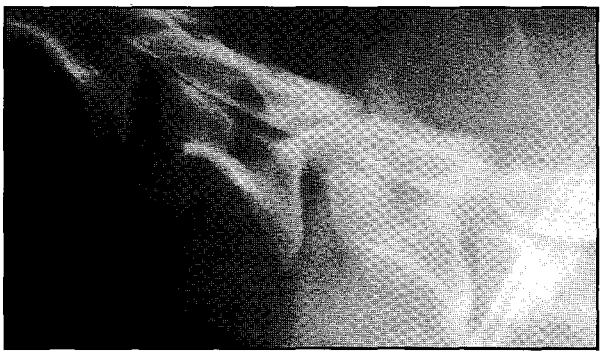

Figure 10.3: *Myelogram of Dobermann with CCSM. There is narrowing of the intervertebral space and dorsal deviation of the ventral contrast column at* $C_{6/7}$*. There is a milder lesion at* $C_{5/6}$*.*

Treatment

Most dogs that show neurological deficits are surgical candidates, but consideration should be given here to non-surgical treatment.

Non-surgical treatment may be indicated in dogs that develop mild neurological deficits following minor trauma. However, surgery should be considered as most dogs will undergo a slow but steady deterioration.

Surgery - a large number of different surgical techniques have been proposed for CCSM, with many achieving a 70 to 80% success rate. The basic types of surgery are:

- Ventral decompression
- Vertebral distraction / fusion
- Dorsal decompression

The main factor governing the choice of surgical procedure is the appearance of the spinal cord on myelography, particularly the traction view. Many lesions, when evaluated by traction, show a combination of both "static" and "dynamic" compression. All of the surgical techniques are technically challenging.

Prognosis

The seriousness of this condition is illustrated by the fact that a quarter of dogs with CCSM in one series were euthanatised within six weeks of surgery, for neurological problems (Seim 1986). Dogs with more than one lesion generally have a worse prognosis than dogs with single lesions, and dogs with chronic tetraparesis have a very guarded prognosis. In contrast, dogs with a sudden onset of signs often respond well to surgery if treated promptly. Most severely tetraparetic dogs that are going to recover will do so within six weeks (Trotter 1985). A useful general estimate of the likely outcome in this condition has been provided by Seim (1986). For dogs with single lesions, about 80% of those that are walking prior to surgery will have a favourable outcome. However, only about 40% of those that cannot walk will recover. These success rates are some 20% lower for dogs with two lesions.

Cervical Disc Disease

Cervical disc disease is a common disorder of dogs. Small breeds, particularly those with chondrodystrophoid characteristics, are commonly affected, but the condition can occur in any dog. Most patients are two years old or more, with a mean of six years. Disc disease is extremely rare in dogs less than one year old.

The predominant clinical sign is severe neck pain, which is unremitting and unresponsive to medication (Figure 10.4). When examining the patient, it is usually not necessary to flex and extend the neck to demonstrate pain; it is adequate to palpate the muscles of the neck, where the tension and pain are evident. Paresis or lameness in a thoracic limb is the most common neurological sign. However, any signs related to cervical spinal cord compression can be seen, including hemiparesis and tetraparesis.

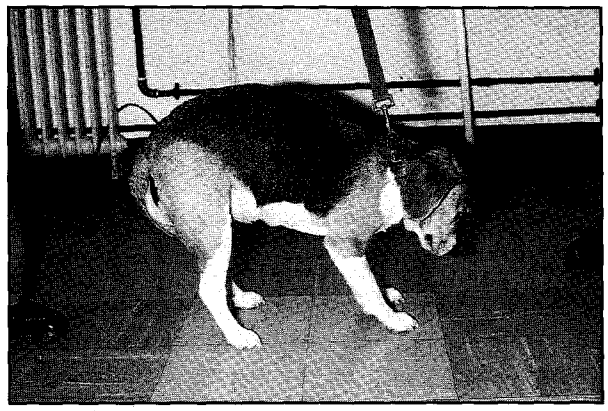

Figure 10.4: *Beagle with severe neck pain related to cervical disc extrusion. (Courtesy Prof. LC Vaughan.)*

Diagnosis

Survey radiography is useful by demonstration of narrowing of the intervertebral space and dorsal displacement of mineralised disc material (Figure 10.5).

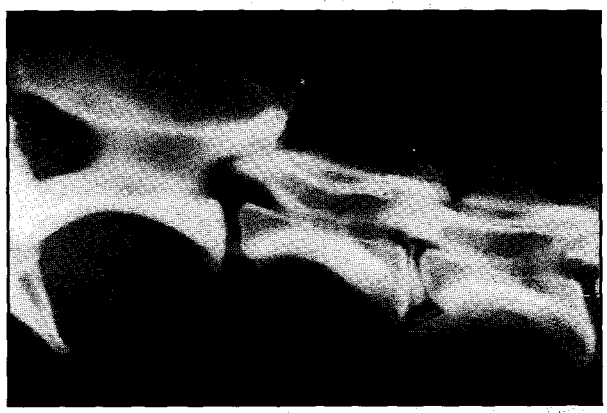

Figure 10.5: *Lateral radiograph demonstrating cervical disc extrusion at $C_{3/4}$.*

Myelography is required if the diagnosis is not apparent on survey films or if there are multiple discs potentially involved (Figure 10.6).

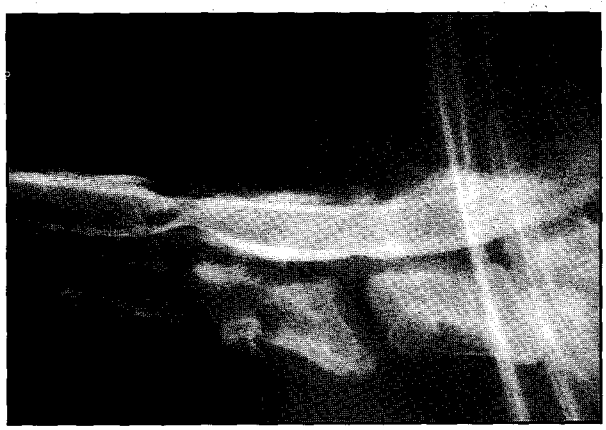

Figure 10.6: *Myelogram of dog with cervical disc extrusion. There is dorsal deviation of the ventral contrast column at $C_{5/6}$. There is column splitting, which indicates an asymmetrical lesion.*

CSF analysis is useful to eliminate inflammatory CNS disease.

Treatment

Non-surgical treatment entails cage rest and use of anti-inflammatory medications. It is appropriate to try this course with any patient, unless marked neurological deficits are present. Progression of signs or lack of response in one to two weeks indicate treatment failure.

Surgical treatment is indicated in the following circumstances:

- Failure of non-surgical treatment
- Marked neurological deficits
- Progressive neurological deficits
- Unremitting pain.

Ventral fenestration or ventral decompression ("ventral slot") are the most frequently performed procedures. General indications for ventral decompression are:

- Presence of neurological deficits
- Myelographic evidence of spinal cord compression
- Failure of fenestration.

Current opinion is that ventral decompression is the optimal method of treatment.

Prognosis

The prognosis for dogs with cervical disc herniations is generally good. Non-surgically treated dogs may have a prolonged convalescent period (several weeks to months) and have an approximately 36% chance of recurrence of signs (Russell and Griffiths 1968). Ventral decompression is superior to fenestration in all neurological parameters; dogs recover more rapidly and recovery rates are higher. Thus ventral decompression is the treatment of choice for most dogs with cervical disc herniations (Fry *et al* 1991).

Calcinosis Circumscripta

Calcinosis circumscripta has been described as a cause of compressive spinal cord dysfunction in young dogs (Dukes McEwan *et al* 1992). Diagnosis is by radiography, a mineralised mass being visible at the site of cord compression. The cause is not known. Surgical decompression may be successful.

Congenital Vertebral Anomalies

Vertebral malformations are common findings in dogs and are occasionally seen in cats. However, they are often clinically insignificant, causing no neurological deficits. Some do cause compressive myelopathy, or may be associated with anomalies of the spinal cord (Bailey and Morgan 1992).

Hemivertebrae are the most common defects seen in dogs, usually in Pugs, Bulldogs and Boston terriers. They are wedge-shaped and may cause spinal deviation in the lateral or dorsoventral plane, depending on the orientation of the wedge. They are the result of failure of formation of part of the vertebral body. Some dogs have butterfly vertebrae; which result from failure of formation of the central part of the vertebra. A skeletal abnormality is often apparent on physical examination. Hemivertebrae may result in a chronic progressive myelopathy, but the site of spinal cord compression should be confirmed by myelography if decompressive surgery is proposed. It may be necessary to stabilise the vertebral column following decompressive surgery. Block vertebrae result from a failure of division of the segments; they rarely cause clinical signs.

Degenerative Myelopathy

("Chronic degenerative radiculomyelopathy" - CDRM)

This is a degenerative condition of the spinal cord of dogs, mostly seen in large breeds and particularly German shepherd dogs. Onset of signs is seen from five years of age. Degenerative changes are found in the spinal cord and nerve roots, mainly affecting the thoracolumbar region. The aetiology is not clear.

Progressive pelvic limb ataxia, loss of conscious proprioception and paraparesis are seen. The neurological examination indicates a T_3-L_3 lesion in most dogs, although some show loss of the patellar reflex, because of the nerve root involvement. Urinary and faecal function is normal, and spinal pain is not seen. Signs in affected dogs progress over several months.

The diagnosis is confirmed by the absence of structural spinal cord disease evident on myelography. Analysis of lumbar CSF usually reveals a moderately raised protein.

A treatment protocol of exercise, vitamins, occasional corticosteroids and aminocaproic acid (not available in the UK) has been suggested (Clemmons 1992). The variable natural history of the disease makes the success of any treatment difficult to judge.

Discospondylitis

Discospondylitis is an inflammatory condition of the intervertebral disc, the vertebral end plates and adjacent vertebral body, usually caused by bacteria. *Staphylococcus intermedius* is the most common agent, with *Brucella canis, Streptococcus spp* and *Escherichia coli* also found. Fungal infections are rare. Large breeds of dogs are most often affected (Kornegay 1986).

Usually the bacteria gain access to the vertebra by haematogenous spread from other foci in the body. Immunosuppression may be a predisposing

factor. Occasional cases associated with foreign body migration, and iatrogenic cases following spinal surgery have also been recognised.

The first clinical sign is usually pain, with concurrent or later development of neurological deficits. Certain sites are predisposed: lumbosacral, caudal cervical, thoracolumbar and mid-thoracic vertebrae. Multiple discs may be involved. Systemic illness is common, typically pyrexia, lethargy, inappetence and cystitis.

Diagnosis is by radiography. Generally the radiographic changes are clearly seen, but occasionally the radiographs will be normal even though infection is present (Figure 10.7). Blood or urine cultures are

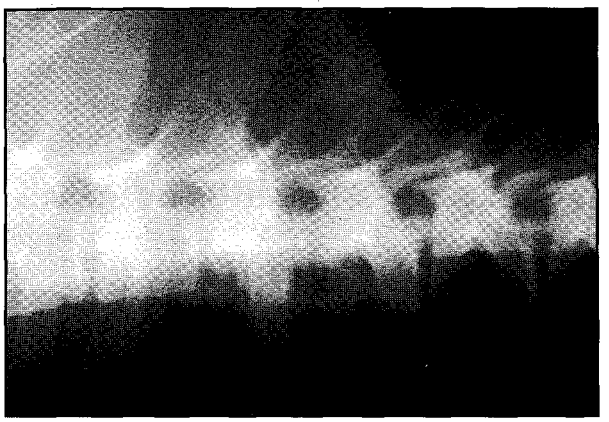

Figure 10.7: *Discospondylitis in cranial thoracic spine. There are two lesions in the adjacent intervertebral spaces.*

positive in about two-thirds of patients. *Brucella canis* titres should be analysed in endemic areas.

Treatment of bacterial discospondylitis is initially by use of appropriate antibiotics. In view of the predominance of *Staph. intermedius*, use of cephradine or cloxacillin are the best initial choices. Ampicillin and amoxycillin are not suitable because the organism is resistant to these drugs through the mechanism of ß-lactamase production. Treatment must be continued for six weeks, even when the response is good. The prognosis is generally favourable.

Surgical curettage of solitary lesions is possible, often leading to rapid resolution of signs. It provides material for culture and promotes blood supply to the affected disc.

If *B. canis* is diagnosed, minocycline (25 mg/kg PO SID for 2 weeks) and streptomycin (5 mg/kg IM or SQ BID for 1 week) or gentamycin (2 mg/kg IM or SQ BID for 1 week) is recommended (Carmichael and Greene 1990). There is potential for zoonotic spread, and recurrence is common. It may be wise to castrate male dogs with *B. canis* infection, as the testes can act as a reservoir of infection.

Dural Ossification

("Ossifying pachymeningitis")

Development of bony plaques in the dura mater of large breed dogs is a common incidental radiographic finding. However, rarely are these plaques the cause of clinical signs and other causes should be explored if neurological deficits are present (Morgan 1969).

Fibrocartilaginous Embolism

("Ischaemic myelopathy")

Fibrocartilaginous embolism (FCE) is a syndrome of acute, severe neurological dysfunction of dogs. It is an important differential diagnosis in cases of disc disease, trauma and other acute spinal conditions (Neer 1992). The emboli have been identified as being composed of fibrocartilage, identical to the nucleus pulposus of the disc. In pathological studies of cases of FCE, emboli may be found in the vasculature of the spinal cord substance or nerve roots. The exact mechanism by which the emboli gain access to these areas is not clear.

Adult dogs of large and giant breeds are most often affected, although the condition does occur in other breeds, particularly the Miniature schnauzer.

Acute, severe neurological presentations occur, often following vigorous exercise or mild trauma. Owners may note a progression of the signs over a period of several hours, perhaps from an initial lameness to eventual paralysis. Pain is not seen on clinical examination, but owners may report that the patient appeared uncomfortable during the development of the condition. Any part of the spinal cord may be affected, and often the signs are markedly asymmetrical.

Confirmation of the diagnosis is by elimination of other causes. Myelography should be performed to rule out compressive spinal cord lesions. Generally, the myelogram is normal, but in some cases of FCE, it will show an intramedullary pattern of spinal cord swelling. Changes in CSF are non-specific.

Treatment is mainly supportive. Use of methylprednisolone, as in spinal trauma, may be useful in the first few hours following onset. Prolonged use of corticosteroids is not indicated.

The prognosis is guarded; UMN deficits often improve, but LMN deficits carry a worse prognosis, because of the involvement of the ventral horn cells in the ischaemic area of spinal cord.

Haemorrage

Haemorrhage and haematoma formation may occur within the spinal cord, in the subarachnoid space or in the epidural space. However, they are rare causes of spinal dysfunction, usually related to trauma or clotting disorders. If spinal haemorrhage is suspected in the absence of trauma, tests for clotting function should be performed. Analysis of CSF may reveal xanthochromia. If fresh blood is seen in a CSF sample, it is most likely to be caused by puncture of a dural vessel rather than a reflection of the underlying disease.

Surgical decompression may be indicated in compressive lesions not associated with clotting disor-

ders. Coagulopathy should be attended to if present, and conservative therapy directed at the spinal lesion.

Inflammatory CNS Diseases

Aseptic Meningitis

("Steroid-responsive meningitis", "Breed-specific meningitis")

Several aseptic meningitis syndromes have been described in dogs, including in Beagles and Bernese mountain dogs (Meric 1993). Clinical signs are typical of meningitis, with dullness, cervical pain, stiff gait and pyrexia. The disease may be acute or have a relapsing pattern. Analysis of CSF reveals marked pleocytosis (WBC counts in the hundreds or even thousands per µl of CSF), mainly comprised of neutrophils, and increased protein concentrations. Infectious agents are not seen in the CSF and culture is negative. The CSF may be relatively normal between bouts of the disease. An immune mediated mechanism is suspected. Treatment is with corticosteroids (prednisolone 2 mg/kg/day initially, later reducing) until clinical signs are controlled. Treatment is continued for several weeks and cessation of treatment may see relapse in some dogs, requiring further steroid administration. The prognosis is generally good, although some dogs experience relapses.

Canine distemper virus infection

Canine distemper virus (CDV) infection is the most common infectious cause of neurological disease in dogs. Demyelination and inflammation occur in certain sites in the CNS. The virulence of the virus strain and the immuno-competence of the dog are important factors in determining the severity of the disease. Other CNS infections may be seen in the face of the immunosuppression related to CDV.

Systemic signs of disease may occur, although this is not a consistent feature (Tipold, Vandevelde and Jaggy 1992). The neurological signs may be multifocal or specifically suggestive of a focal lesion, and may be acute in onset. Confirmation of a diagnosis of CDV infection ante mortem is difficult - analysis of CSF is the most useful test. Treatment is restricted to managing the clinical signs and providing supportive care. Corticosteroids may be useful in some patients, but the prognosis is poor.

Granulomatous meningoencephalomyelitis

("Reticulosis", GME)

This is an inflammatory disease of the CNS of unknown aetiology. Any part of the CNS may be involved, either in a focal or diffuse form. Clinical signs are typical of meningoencephalomyelitis and onset is usually between three to seven years of age. Spinal cord syndromes may be seen alone or as part of a multifocal presentation. The course is usually chronic, but some cases show a rapid decline. Analysis of CSF reveals moderate, mainly mononuclear pleocytosis with increased protein, but the findings are non-specific. Some dogs with spinal cord involvement have myelographic patterns suggestive of intramedullary lesions. Treatment with immunosuppressive doses of corticosteroids may lead to improvement (prednisolone 1 to 2 mg/kg per day). The long term prognosis is poor.

Other infectious agents

Infection of the spinal cord by organisms other than viruses is rare in dogs. Spinal infections are often associated with brain involvement, causing multifocal neurological signs. Many organisms have been implicated, including bacteria, fungi, rickettsia and prototheca species; the distribution of many of these organisms is regional. The signs are typical of inflammatory CNS disease as described above. Some show signs of intracranial disease, typically in rickettsial infections where seizures, dullness, depression and vestibular signs are seen. Pelvic limb hyperextension is often seen in toxoplasmosis or neosporosis. Systemic signs of infection may be apparent, for example, gastrointestinal disturbance or respiratory signs, which may indicate the means of entry into the CNS. Patients may be pyrexic, but this is variable. Confirmation of the diagnosis is usually by CSF analysis. Pleocytosis is variable, but very high cell counts (in the thousands per µl) may be seen, mostly composed of neutrophils, and eosinophils may also be present. Organisms may be seen in the CSF. Culture may be attempted but is often unrewarding. Serological testing may be useful in some infections, for example, in rickettsial infections or cryptococcosis (Greene 1990).

Those rare patients where bacterial infections are identified should be treated with antibiotics. The bacterial sensitivity and CNS penetration of the drug must be considered in choosing an antibiotic (Chapter 6). Fungal infections are difficult to treat, but amphotericin B, fluocytosine and ketoconazole have been suggested. Rickettsial infections are treated with tetracyclines, preferably doxycycline, or chloramphenicol (Greene 1990). Protozoal infections may be treated with clindamycin.

The use of corticosteroids in meningomyelitis is controversial. They are certainly contraindicated in fungal infection, but may have a role in bacterial infections. The potential consequences of corticosteroid use must be considered before they are administered.

Leukoencephalomalacia

Leukoencephalomalacia is a degenerative CNS disease, reported only in Rottweilers in the USA, The Netherlands and Australia. There is malacia throughout the spinal cord, particularly in the cervical region, due to demyelination and cavitation. The aetiology is unclear (Chrisman 1992).

Affected dogs show clinical signs from $1^1/_2$ to 4 years of age. There is pelvic limb ataxia and hypermetria, progressing through paraparesis to tetraparesis over a period of months. Conscious proprioceptive deficits are marked. Limb reflexes are intact or hyperactive.

Differentiation from neuroaxonal dystrophy and other CNS conditions is important. All routine diagnostic tests are normal in leukoencephalomalacia. The major differential features are the presence of conscious proprioceptive deficits in leukoencephalomalacia, and tremor seen in neuroaxonal dystrophy.

There is no treatment and the prognosis is poor, most dogs with leukoencephalomalacia being euthanatised within one year of presentation.

Lumbosacral Disease

The clinical signs of lumbosacral lesions differ from those seen at other locations of the spine, because of the unique anatomical structure of the region. The vertebral canal of the caudal lumbar spine contains not spinal cord but the cauda equina - the collection of peripheral nerves that course caudally from the terminal spinal cord. The lumbosacral joint is a site of considerable transfer of forces and is thus susceptible to degenerative changes.

Lumbosacral lesions can cause pelvic limb gait abnormalities, lameness, or LMN neurological deficits. The lower urinary tract, tail and anus may be affected. Pain is a common feature.

Various disease processes can affect the lumbosacral spine and the neurological structures in this region. Larger breeds of dogs, particularly German shepherd dogs, tend to be most frequently involved, although occasionally small dogs are affected. Young, working dogs that have been heavily trained are particularly prone to this disorder (Wheeler 1992).

A number of congenital and degenerative abnormalities may combine to cause compression of the cauda equina or L_7 nerve roots. Tumours, discospondylitis and fractures can also occur

Pain, lameness and reluctance to exercise are the most common clinical signs. Acute injuries may be associated with severe pain. Neurological problems range from no deficits, through mild paresis with conscious proprioceptive deficits, to severe paraparesis, tail paralysis, and urinary and faecal incontinence. Dogs with chronic degenerative lumbosacral lesions may present with non-specific clinical signs, but low back pain is quite different from that seen in thoracolumbar lesions. Diagnosis of lumbosacral disease depends on recognising the clinical signs described here and on a careful physical examination, which will pinpoint the focus of pain.

Diagnosis

The vague signs may make accurate diagnosis difficult in some patients, as other diseases could be causing or complicating the picture. A thorough physical, orthopaedic and neurological examination is essential, including a rectal examination. Hyperaesthesia is a frequent finding. Direct pressure over the lumbosacral joint may pinpoint a specific focus of pain.

Radiography

Survey radiographs are difficult to interpret, because many clinically normal dogs have radiographic abnormalities of the lumbosacral junction. Conversely, occasional dogs with lumbosacral disease will have normal survey radiographs. It is essential that the patient be anaesthetised when radiographing the lumbosacral joint. Some specific diseases may be visible on survey radiographs, for example, discospondylitis (Figure 10.8).

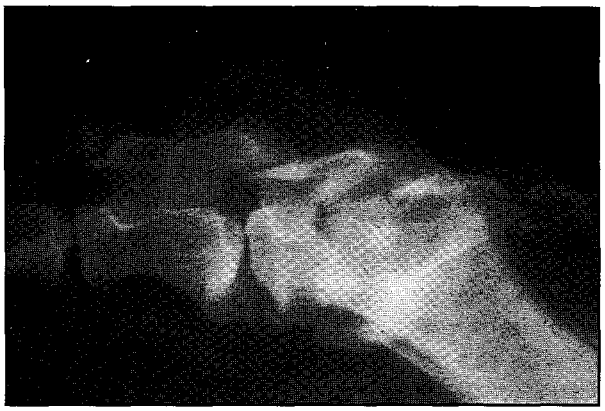

Figure 10.8: *Discospondylitis at lumbosacral junction.*

Myelography is useful in assessing the low lumbar spine (Figure 10.9). Cervical injection is preferred.

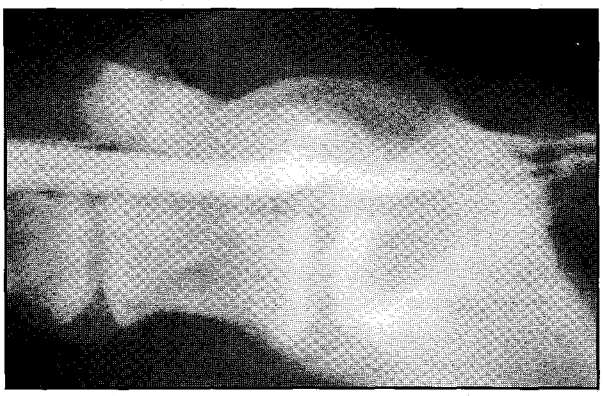

Figure 10.9: *Myelogram demonstrating cauda equina compression at lumbosacral junction.*

Epidurography may demonstrate some lesions, usually by obstruction or dorsal deviation of the column.

Treatment

Non-surgical treatment - most dogs are initially treated non-surgically with rest and anti-inflammatory medication. If pain is the main clinical sign, this course may be successful. A lengthy period of inactivity can lead to improvement.

Surgical treatment is indicated in dogs with motor deficits, or where non-surgical treatment has failed. Decompression of the cauda equina and spinal nerves is achieved by dorsal laminectomy and foramenotomy.

Prognosis

Laminectomy and foramenotomy provide rapid relief from pain in most dogs. Similarly, lameness and mild neurological deficits usually recover rapidly. More severe LMN deficits carry a less favourable prognosis (Chambers 1989).

Multiple Cartilaginous Exostoses

("Osteochondromatosis")

Cartilaginous exostoses may cause spinal cord compression at any site of the vertebral column. Lesions may also occur on the ribs and limb bones. There is abnormal differentiation of cartilage cells in bones that develop by endochondral ossification, leading to the production of large masses composed of a thin cortex lined by cartilage, and a core of cancellous bone. The aetiology is unclear (Gambardella, Osborne and Stevens 1975). The masses continue to grow until skeletal maturity is reached. Diagnosis is by radiography. Surgical decompression of compressive lesions may be necessary.

Neoplasia

Spinal tumours are uncommon causes of spinal disease. Older animals are usually affected, although certain tumour types do occur in young individuals, notably lymphoma in cats.

Clinical signs produced by tumours of the spine are the same as those seen for any spinal disorder. Patients often have a fairly typical pattern of initial non-specific discomfort, followed by development of progressive neurological deficits and more definitive evidence of spinal pain. Marked muscle atrophy is often seen caudal to the lesion. Occasionally there is a precipitous decline in the neurological status.

Tumours involving the brachial or lumbosacral plexus may present initially as a progressive unilateral lameness (Chapter 11). The involvement of other body systems in diffuse neoplasia or metastasis may cause clinical signs unrelated to the nervous system.

Spinal tumours can be diagnosed relatively easily using standard methods. Survey radiographs and myelography are most useful. The myelogram should provide information about the location of the tumour, and its position within the vertebral canal (Chapter 5). A CSF sample should be collected, as occasionally neoplastic cells will be identified.

There are a large number of tumour types that affect the spine; many are only reported in small numbers, and these have been reviewed (Bagley *et al* 1993). Spinal tumours are classified according to their location in the spine:

- Extradural
- Intradural-extramedullary
- Intramedullary

Extradural tumours are the most prevalent type in dogs, accounting for approximately one-half of the cases; most are vertebral tumours or metastases. Intradural-extramedullary tumours make up one-third; they are mainly meningiomas or nerve sheath tumours. Intramedullary tumours account for the remainder (Prata 1977).

Treatment

Treatment is not possible in every animal with a spinal tumour, but an aggressive approach will prove rewarding in some patients. Vertebral body tumours are rarely good candidates for treatment, with the exception of myeloma.

Medical treatment of spinal tumours is unlikely to prove curative. Palliative therapy (analgesics, anti-inflammatory agents) may be used, relieving clinical signs for relatively short periods. In lymphoma, chemotherapy alone may be employed if the diagnosis is reached without surgical intervention, and should be used following surgery (Gorman 1991). Medical treatment also has a role in surgical patients as spinal tumours are frequently painful and postoperative analgesia is required.

Radiation treatment is of value, mainly as an adjunct to surgery, although it may have a primary role, for example, in lymphoma (Dobson 1991).

Surgical treatment should be considered in most patients. There are two aims: to collect tissue for histopathological evaluation and to improve spinal cord function by tumour removal and decompression. Surgical intervention is most appropriate where the mass is in the extradural space, or is in an intradural - extramedullary location.

Prognosis

In some circumstances, where the tumour is not amenable to treatment because of its location, or where a "pathological" fracture has occurred, euthanasia is indicated. Remission can often be achieved for lymphoma in both dogs and cats, leading to a significant degree of neurological recovery. Cats usually succumb eventually to systemic effects of the disease (Lane and Kornegay 1991). Some dogs that have meningiomas resected have lengthy remission periods (Fingeroth, Prata and Patnaik 1987). Spinal tumours do have a tendency to recur locally, usually because of incomplete resection.

Neuroaxonal Dystrophy

Neuroaxonal dystrophy is a degenerative CNS disease seen mainly in Rottweilers, but also occasionally reported in cats. It is thought to be an autosomal recessive condition in the Rottweiler. Axonal dystrophy with axonal spheroids is seen in parts of the CNS, including the dorsal horn grey matter of the spinal cord, and the gracile, cuneate and dorsal spinocerebellar tract nuclei. Cerebellar atrophy may also be seen. The aetiology is unknown (Chrisman 1992).

Affected dogs show clinical signs from puppyhood, but they may not be noticed until the dog is adult. There is pelvic limb ataxia and hypermetria of the thoracic limbs. Conscious proprioception is normal. Limb reflexes are intact or hyperactive. Head incoordination, tremor, positional nystagmus and loss of menace response (due to cerebellar involvement) develop later, often after several years. Weakness is not seen.

Differentiation from leukoencephalomalacia and other CNS conditions is important. Routine diagnostic tests are normal. There is no treatment and the prognosis is poor, although affected dogs may survive as active pets for several years.

Pilonidal Sinus

("Dermoid sinus", "epidermoid cyst")

In pilonidal sinus the skin over the dorsal midline is inverted and, in some dogs, communicates with the dura mater. Rhodesian ridgebacks and Shih Tzus have a high incidence. Infection from the cyst may extend to the spinal cord, causing meningitis and myelitis with associated clinical signs. Diagnosis is based on the clinical signs. If a cyst is suspected to be in communication with the vertebral canal, fistulography may be performed, but it is important to use a non-ionic contrast medium. Infected lesions are treated by antibiotics and surgical excision; it may be necessary to perform a laminectomy to retrieve all the tissue. Careless exploration of this type of lesion, without a full appreciation of its extent, can lead to the development of marked neurological deficits.

Sacrocaudal dysgenesis

Dogs with congenital tail defects often have vertebral abnormalities of the sacrum and caudal vertebrae. Pugs and Bulldogs are most often affected. The vertebral abnormalities may themselves result in neurological signs of the pelvic limbs and viscera (urinary tract and anus). There may be malformations of the spinal cord, for example, spina bifida with associated skin lesions.

Diagnosis is suspected from the clinical signs. Radiography will demonstrate vertebral abnormalities and myelography may reveal spinal cord malformations. Treatment is not possible and the prognosis is poor.

Spina Bifida

This is a developmental defect resulting from failure of fusion of the embryonic vertebral arch. There may be protrusion of the meninges or spinal cord into a meningocoele, a myelocoele or a meningomyelocoele; this is termed spina bifida aperta. Alternatively, there may be no protrusion of nervous tissue - termed spina bifida occulta (Wilson 1982). The aetiology is unknown, but there is a high incidence in English bulldogs.

The condition occurs most commonly in the caudal lumbar spine. Clinical signs indicative of L_4-S_3 spinal cord dysfunction are seen. Radiography may reveal defects in the dorsal vertebral arch, for example, paired spinous processes, and myelography may demonstrate a meningocoele. Treatment is not possible.

Spinal Dysraphism

("Myelodysplasia")

Malformations of the spinal cord have been described in several breeds of dogs, particularly Weimaraners (Van den Broek *et al* 1991). Various lesions of the central canal, grey matter, dorsal sulcus and ventral fissure have been described. The condition is inherited in Weimaraners. Signs indicative of T_3-L_3 spinal cord disease are seen in puppies. A "bunny-hopping" pelvic limb gait is often seen. Abnormalities of the hair coat, a depression of the sternum and head tilt may be seen. The signs may or may not be progressive, and there is no treatment.

Spondylosis Deformans

Spondylosis deformans is a common radiographic finding in older dogs, but rarely is it associated with clinical signs. Generally osteophytes develop ventrally and laterally on the vertebral body, and may grow to the point that they cross the intervertebral space. The anticlinal region, thoracolumbar junction and lumbosacral joint are particularly affected. Where these changes are seen at the lumbosacral joint they may be related to clinical signs of lumbosacral disease. However, this diagnosis should not be reached on the basis of survey radiographs alone, as such changes are seen in many normal dogs (Figure 10.10). It is important to differentiate spondylosis deformans from the changes seen in discospondylitis.

Figure 10.10: *Spondylosis deformans. This was an incidental finding and is rarely the cause of clinical signs*

Storage Diseases

Lysosomal storage diseases occur where there is a defect of metabolism because of a dysfunction in a specific enzyme pathway. They are relatively common in dogs and frequently cause neurological signs, which may appear to be related to a spinal lesion. They are seen from early in life and are progressive. The majority are inherited in an autosomal recessive pattern. Diagnosis is based on various biopsies, depending on the nature of the disease. There is no treatment, and the prognosis is poor (See Chapter 8).

Syringomyelia

Syringomyelia and hydromyelia are fluid-filled cavitations of the spinal cord and central canal. Syringomyelia may be associated with any type of acquired spinal cord lesion, although the cause is not known. Hydromyelia is often associated with congenital spinal malformations, and may be the result of altered CSF pressures. Syringomyelia may be seen in Weimaraners with dysraphism. The cavitation of the spinal cord in both conditions may be progressive. Clinical differentiation is not possible. Clinical signs of spinal cord dysfunction depend on the location of the lesion in the vertebral column. Associated skeletal changes including torticollis or scoliosis may be seen (Child, Higgins and Cuddon 1986). MRI may aid in making the diagnosis.

Thoracolumbar Disc Disease

Thoracolumbar disc disease is a common condition that affects predominantly chondrodystrophoid breeds of dog. It reaches a peak incidence between three and six years of age. Non-chondrodystrophoid breeds are less frequently affected, and usually only after middle age. Most thoracolumbar disc lesions occur between $T_{11/12}$ and $L_{1/2}$ inclusive.

Spinal hyperaesthesia, neurological deficits in the pelvic limbs and urinary dysfunction are seen. Pain alone can be misinterpreted as being abdominal in origin. Neurological deficits range from mild ataxia and paresis, to paraplegia, which may be accompanied by depressed or absent deep pain sensation caudal to the lesion. In many patients there is a panniculus reflex "cut-off".

Progressive myelomalacia

Progressive myelomalacia ("the ascending syndrome") affects 3-6% of dogs with severe neurological deficits related to thoracolumbar disc disease (Davies and Sharp 1983). It usually has a delay in onset of several days after the dog becomes paralysed, and may only become evident during the postoperative period. Profound hyperaesthesia and toxaemia are the hallmarks of the condition. The clinician should be suspicious of this problem if a paralysed dog becomes depressed, there is progressive loss of pelvic limb reflexes, and the level of panniculus reflex "cut-off" moves cranially. Extensive epidural and subarachnoid haemorrhage occurs, together with epidural fat necrosis and both arterial and venous thrombosis. As soon as this condition is recognised, euthanasia should be performed on humane grounds, as patients will die within a few days, usually of respiratory failure.

Diagnosis

Survey radiographs indicate whether disc disease is present, but are only accurate in identifying the exact location in two thirds of disc herniations (Kirberger, Roos and Lubbe 1992). Survey radiographs should not be used as the sole means of confirming the diagnosis if decompressive surgery is planned.

Myelography is required for a more definitive diagnosis. Lumbar myelography is preferred, because there is often considerable cord swelling, and contrast medium must be injected with some force to outline the lesion.

Lateral and ventrodorsal radiographs should be taken of the region of interest. It is often possible to determine on which side of the vertebral canal the disc material lies from the clinical signs and the ventrodorsal myelogram (Figure 10.11). If there is doubt, oblique views should be taken.

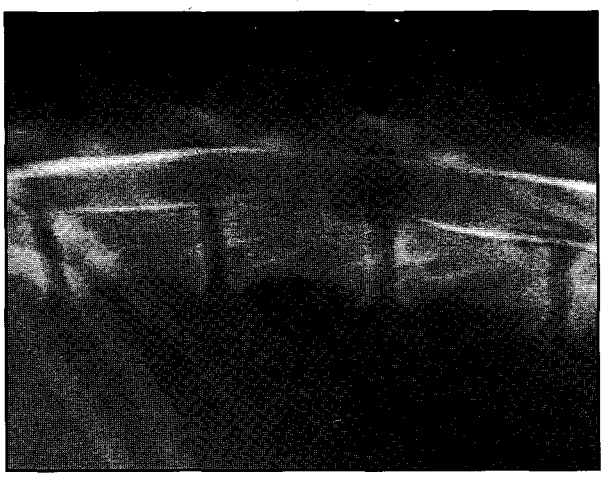

Figure 10.11 (a): *Lateral myelogram.*

Cerebrospinal fluid analysis should be analysed to rule out other conditions.

Treatment

Non-surgical treatment - strict cage rest is the overriding principle, although judicious use of anti-inflammatory medications can be helpful. The animal must rest quietly in a confined space for at least two weeks, during which time it should only be removed to allow it to urinate and defecate. *A short course of anti-inflammatory drugs without cage rest does not constitute effective non-surgical treatment.* A high proportion of dogs referred for emergency decompressive surgery have been treated in the preceding

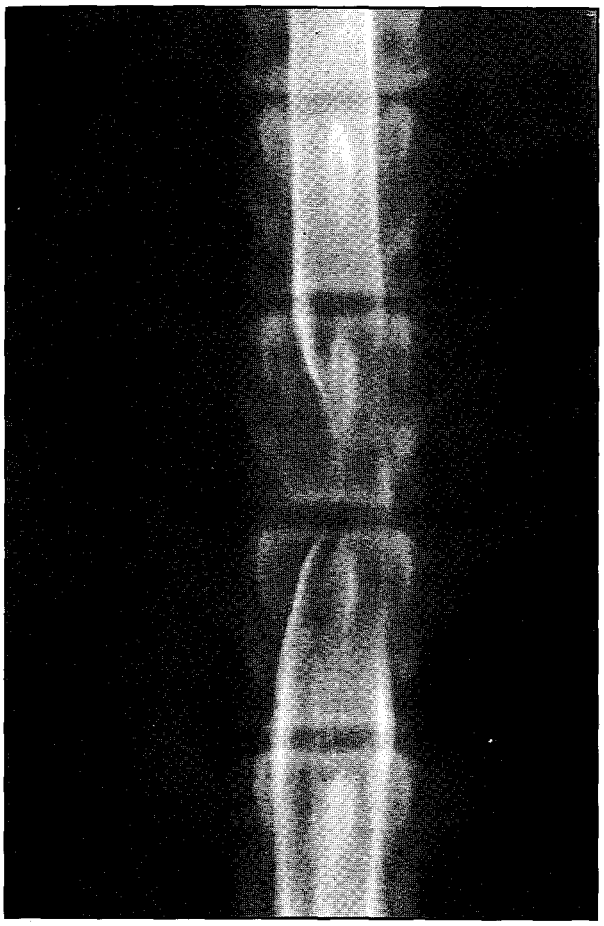

Figure 10.11 (b): Ventrodorsal myelogram. Dachshund with thoracolumbar disc extrusion. There is thinning of both dorsal and ventral columns on the lateral projection. It is not possible to determine the location of the lesion on this projection alone. The ventrodorsal view reveals that the compression is extradural, on the right side of the dog (left of the radiograph).

days or weeks with corticosteroids, but with no cage confinement. The corticosteroids relieve the dog's discomfort but often make it much more active. This renders the dog very susceptible to further herniation of disc material and subsequent development of severe neurological deficits. Anti-inflammatory medication may be withheld during the initial period of non-surgical treatment in order to encourage the animal to rest.

Surgery

Hemilaminectomy is the treatment of choice for most dogs with neurological deficits of grade 2 or more (see Chapter 3). Decompression should be performed as soon as possible after the onset of neurological signs, especially for dogs with severe deficits. This is crucial in animals with depressed or absent deep pain sensation. Those with absent deep pain sensation should be regarded as emergencies, requiring surgery within 24 hours to have the best chance for a successful outcome. Reasonable results can still be obtained if surgery is performed within 48 hours, but after three days the results are dismal. The rate of recovery is faster after hemilaminectomy than after fenestration or conservative treatment.

Postoperative care

It is important to ensure that the bladder is regularly emptied of all urine. Pharmacological management of urination should be used whenever urinary function is impaired (Chapter 12).

Prognosis

The prognosis for a functional recovery is very good for dogs with grade 1, 2, and 3 lesions. Paralysed dogs with intact deep pain sensation show a similar overall response following either hemilaminectomy or fenestration. When hemilaminectomy is performed within 48 hours of the onset of a grade 5 lesion, the animal has an approximately 50% chance of making a functional recovery. Importantly, recovery is faster with decompressive surgery in dogs with significant neurological deficits.

Trauma

Trauma can result in a variety of spinal lesions. Diagnosis should be straightforward from the history and physical findings. A thorough and meticulous physical examination is essential at an early stage as many animals have additional non-neural injuries, which could be overlooked. Cardiovascular, urinary and biliary complications are most common.

After the initial assessment (including deep pain evaluation) the patient is given analgesics. The narcotic agonists are preferred unless there is concomitant respiratory depression or head injury. Analgesia should be combined with some form of stabilisation for the injury, so that the animal does not damage itself further. If presented within eight hours of injury, high-dose methylprednisolone sodium succinate should be given by slow intravenous injection.

Methylprednisolone sodium succinate - after acute injury, the blood supply to the spinal cord is progressively reduced. When the injured tissue is reperfused, massive amounts of highly reactive chemicals called free radicals are liberated. These free radicals are especially damaging to the plasma membrane of cells via a process called lipid peroxidation. Free radical-induced lipid peroxidation is now recognised as a key pathophysiological mechanism for irreversible tissue loss following spinal cord trauma and ischaemia. Methylprednisolone has some protective effect at high doses. The suggested dosage regime is an initial IV bolus of 30 mg/kg methylprednisolone , followed by 15 mg/kg IV 2 and 6 hours later, then 2.5 mg/kg IV per hour for a further 24-48 hours (Brown and Hall 1992).

Other corticosteroids can cause gastrointestinal bleeding in as many as 15 per cent of neurosurgical

patients, with mortality rates of up to 2 per cent (Moore and Withrow 1982). Dexamethasone is most likely to cause these problems, yet there is little evidence that this drug has benefit in CNS injury and it is of doubtful value in experimental acute spinal cord trauma. Thus, routine glucocorticoid therapy in spinal patients is strongly discouraged. Similarly, combinations of steroid and non-steroidal anti-inflammatory agents have no therapeutic advantage, but a high incidence of serious complications. *These agents should never be used in combination.*

Neurological examination

The neurological examination is essential to localise the deficit, to identify multiple spinal lesions, and to determine the prognosis. The single, most important prognostic factor following spinal trauma is the presence or absence of deep pain sensation. If deep pain is absent caudal to a traumatic lesion, the prognosis for return of neurological function is very poor. (Analgesics should only be given after deep pain has been assessed, as they could alter the findings.)

Radiography

Survey radiographs are taken after the lesion has been localised. Radiographs are no substitute for the neurological examination; it is not possible to estimate the neurological status from the radiographs alone. Lateral views of the area of spine where the lesion is located are taken first. Dorsoventral radiographs are best taken by the horizontal beam view. With the possibility of multiple fractures in mind, some neurologists advocate making survey radiographs of the whole spine, but multiple vertebral fractures are not common.

Myelography is recommend for potential surgical candidates.

Treatment

Choice of therapy depends initially on the prognosis suggested by the neurological examination.

If there is no deep pain sensation, the prognosis is poor. Severe shock and hypotension can exacerbate the neurological deficit, so it may be worth reassessing a patient lacking deep pain sensation after allowing a 24 to 48 hour period of circulatory support.

In patient with intact deep pain sensation, a decision must be made between surgical and non surgical management. This is governed by clinician preference, expertise, client wishes and finances. The following are general recommendations for these patients:

- Severe spinal cord compression, or vertebral instability, should be relieved surgically whenever possible. Reduction of malalignment and rigid fixation are the goals of surgery.
- Decompression should be performed if there is radiographic or myelographic evidence of marked spinal cord compression. Routine decompression of spinal trauma cases that are not suffering compression is not indicated.
- If decompression is performed, the vertebral column must always be stabilised by internal fixation.

Conservative treatment - animals with fracture / luxations in the cervical or lumbosacral regions often respond well to cage confinement for four to six weeks.

External splints are useful and make patient handling easier than in conservative treatment alone.

Surgery

Decompression is best achieved in the thoracolumbar spine by hemilaminectomy, if possible, as this has the least destabilising effect on the spine. Decompression is only indicated if there is evidence of persistent spinal cord compression, for example, by myelography. Many methods of spinal stabilisation have been described. Most dorsal methods have a tendency to fail. The preferred method is use of metal implants and bone cement (Wheeler and Sharp 1994) (Figure 10.12).

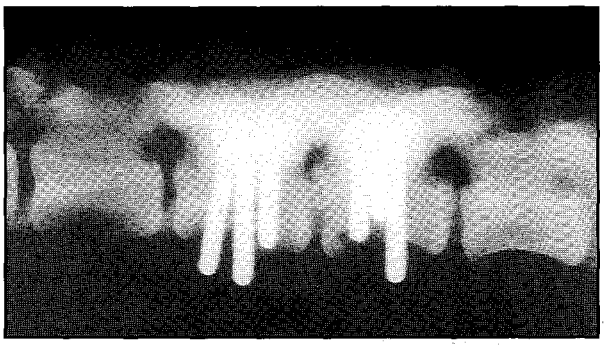

Figure 10.12 (a): *Repair of spinal fracture/luxation with metal implants and methylmethacrylate bone cement.*

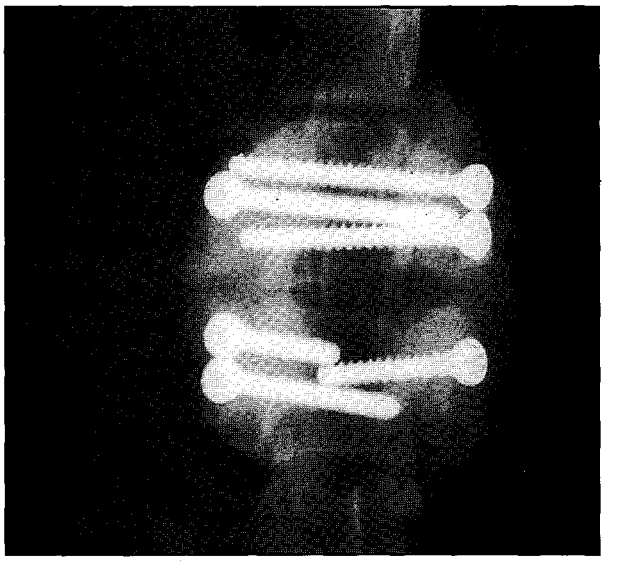

Figure 10.12 (b): *Repair of spinal fracture/luxation with metal implants and methylmethacrylate bone cement.*

Prognosis

The prognosis is similar to that given for thoracolumbar disc disease, although grade 5 deficits rarely recover after trauma.

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CHAPTER ELEVEN

Neurological Deficits in One Limb

Nicholas J. H. Sharp

INTRODUCTION

A number of conditions may present with a neurological deficit to one limb. If this deficit results in weakness of the limb, then the correct term is **monoparesis.** If the motor deficit is complete, and the animal is unable to move the limb at all then the correct term is **monoplegia.**

The term **mononeuropathy** refers to a condition affecting one specific peripheral nerve. A severe mononeuropathy of the sciatic nerve will, of course, result in an obvious monoparesis of the affected pelvic limb. However, that limb is not totally paralysed or monoplegic as the other peripheral nerves to that limb are functional and the animal can still move the limb.

THORACIC LIMB

Anatomy of the Brachial Plexus and Thoracic Limb Innervation

Detailed descriptions are available in standard veterinary anatomy and neurology texts. However, a working knowledge of the anatomy of this area does not require great detail, yet will considerably aid diagnosis. The brachial plexus is derived from spinal cord segments C_6 to T_1, and less frequently C_5 and/or T_2 also make a contribution. We may remember the order in which the main peripheral nerve arise from the plexus as:

Suprascapular	Musculocutaneous
$C_{6(7)}$	$C_{7(6,8)}$
Radial	Median/Ulnar
C_7, $C_8(T_1)$	C_8, $T_1(T_2)$

The nerve arising at the most caudal part of the plexus tends to innervate the most caudal muscles, and is derived from the most caudal nerve root (Figure 11.1). The opposite is true cranially.

The area of mixing of the contributing spinal nerves and the exiting peripheral nerves is called the **common brachial plexus bundle.**

Important nerves of the plexus

To consider the most important nerves of the plexus individually:

Suprascapular nerve - supplies motor fibres to the spinatus muscles, on the lateral aspect of the scapula, which provide lateral support to the shoulder joint.

Musculocutaneous nerve - supplies motor fibres to the muscles that flex the elbow (e.g. biceps brachii). It supplies sensation to the medial antebrachium. The autonomous test site (the region innervated solely by that nerve, with no overlap from other nerves) lies just distal to the medial epicondyle of the humerus (Bailey and Kitchell 1987).

Radial nerve - is the most important nerve of the thoracic limb. It innervates the extensor muscles of the triceps group, which fix the elbow, and the muscles that extend both the carpus and digits. It is sensory to the whole cranial aspect of the antebrachium and foot, except the fifth digit, and the test site is on the dorsal aspect of the third digit.

Median and ulnar nerves - together innervate the muscles that flex the carpus and digits. They supply sensation to the caudal aspect of the antebrachium and foot. Sensation can be tested just distal to the olecranon and on the lateral aspect of the fifth digit.

The other peripheral nerves arising from the brachial plexus, such as the axillary and subscapular, are obviously important but need not be considered clinically in the evaluation of plexus dysfunction.

Two other important components of the brachial plexus are the lateral thoracic nerve and sympathetic nerves. Both arise from the caudal portion of the plexus. The relevance of these will become apparent in the section on neurological examination.

Lateral thoracic nerve - arises from C_8 and T_1 spinal cord segments and innervates the cutaneous trunci muscle. It is responsible for the motor portion of the panniculus reflex on the ipsilateral side of the body.

Sympathetic nerves - to the head and neck leave the spinal cord through the T_1 and T_2 spinal nerves. These enter the stellate ganglion near the first rib, from which axons pass rostrally along the sympathetic portion of the vagosympathetic trunk. Sympathetic stimu-

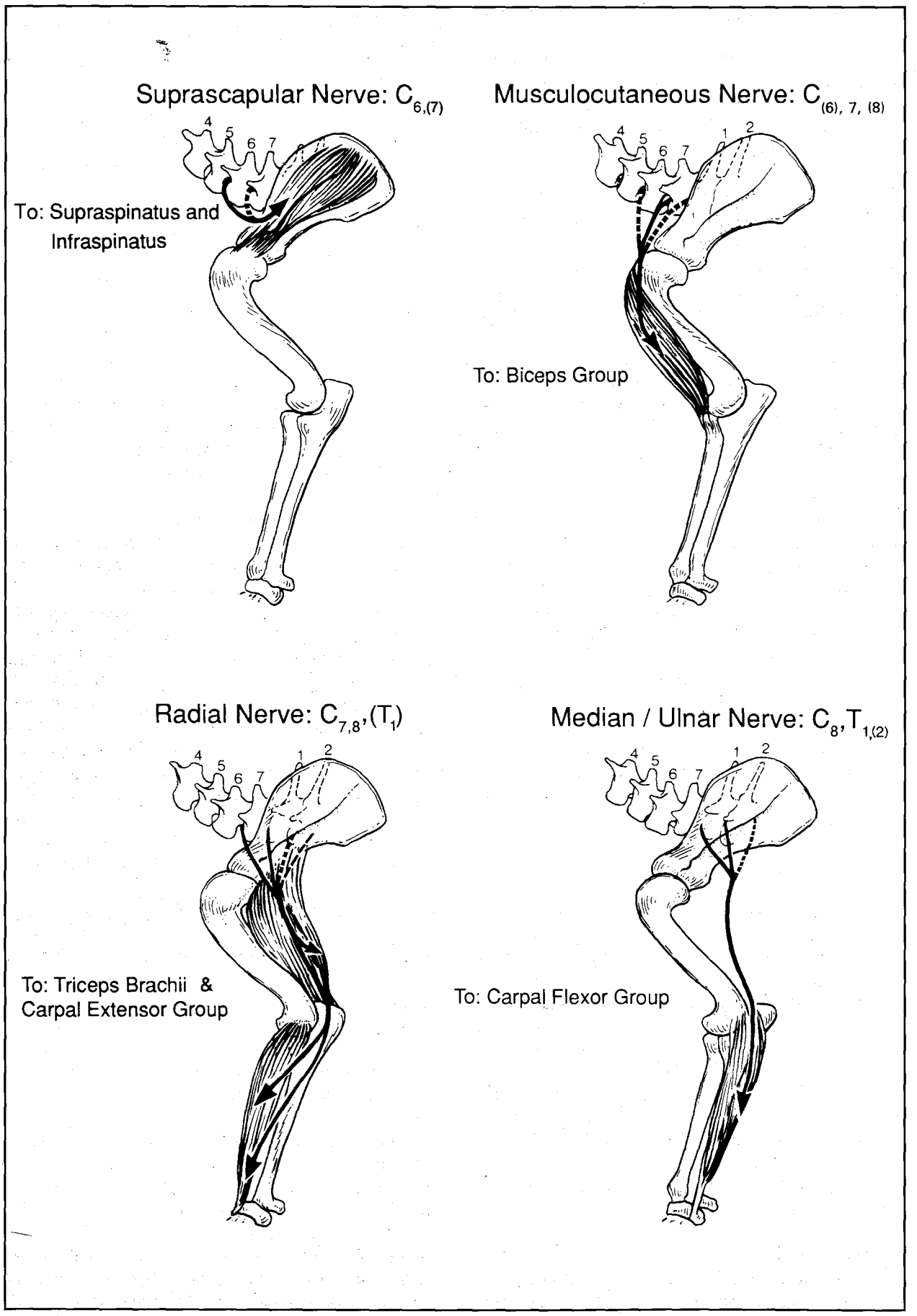


Figure 11.1: Diagram to show the main peripheral nerves arising from the brachial plexus.

lation causes mydriasis and retraction of the third eyelid.

The panniculus reflex and Horner's syndrome are very important features of the neurological examination, both for the identification and characterisation of brachial plexus injuries and for their differentiation from radial paralysis.

Neurological Examination

The degree of involvement of the ipsilateral pelvic limb and of the contralateral limbs should be assessed. The deficit must be characterised as either UMN or LMN (see Chapter 3). A sensitive indicator of mild LMN disease in the thoracic limb is weakness in carpal flexion.

The animal should be examined for evidence of Horner's syndrome and panniculus reflex loss in order to differentiate a lesion affecting the spinal cord, plexus, or nerve roots, from one involving only the peripheral nerve trunks.

Panniculus reflex - this is best considered as two identical reflexes, one for each side of the body. The sensory component of the reflex has a dermatomal input over one side of the trunk. The motor component arises from the ipsilateral spinal cord segments C_8 and T_1 and innervates the ipsilateral cutaneous trunci muscle via the lateral thoracic nerve (Figure 3.3). A unilateral spinal cord lesion or avulsion of the nerve roots at C_8 and T_1 will therefore abolish the ipsilateral panniculus reflex. Provided that the contralateral C_8 and T_1 spinal cord segments and nerve roots are intact, a consensual response will be present. This occurs because ascending sensory stimuli can cross to the contralateral spinal cord below the level of the lesion (see **Panniculus reflex**, Chapter 3).

Horner's Syndrome - Complete Horner's syndrome comprises miosis, enophthalmos, ptosis and prolapse of the third eyelid and is usually very obvious. Lesions affecting T_1 and T_2 nerve roots nearly always result in a partial Horner's syndrome where only a miotic pupil occurs. This is much more subtle and can easily be missed, particularly in animals with a dark iris. The pupils should be assessed from a distance of two feet from the animal's face using a bright ophthalmoscope (Figures 9.6 and 9.7, page 128). The reflection from the tapetal fundus will clearly delineate the two pupillary apertures and allow comparison of the diameters. Mild unilateral miosis can be detected in this manner (see Horner's syndrome, page 136 and Figures 9.15 and 9.16).

Lesion Localisation

From the neurological examination it should be possible to categorise the monoparesis, and thus localise the lesion to one of the following areas (Table 11.1).

Table 11.1.

A	C_1-C_5 spinal cord	UMN signs, other limb(s) involved
B	C_6-T_2 spinal cord	LMN signs, other limb(s) involved
C	C_6-T_2 nerve roots and brachial plexus	unilateral LMN signs, ± Horner's syndrome or panniculus reflex loss
D	Radial nerve	unilateral LMN signs, no Horner's syndrome or panniculus reflex loss

A myelogram is used to help differentiate a lesion affecting the spinal cord (A and B) from one affecting the peripheral structures (C and D). Lesions affecting these four areas are considered below.

Assessing the severity of a lesion

As well as localising the lesion, another very important role of the neurological examination is to provide some idea about the severity of the deficit.

The diameter of a nerve fibre has a direct bearing on the susceptibility of that fibre to compression. This is true whether the nerve fibre is in the central or peripheral nervous system. Large myelinated fibres (mainly those supplying proprioceptive function) are the most sensitive to injury. The slightly smaller myelinated fibres controlling motor function are the next most susceptible. Small non-myelinated fibres supplying nociception (deep pain sensation) are the most resistant to compression. Therefore, with increasing compression of any nerve, proprioceptive function will be compromised initially, followed by impaired motor function, and finally deep pain sensation will be lost. The presence of intact deep pain sensation to a limb implies a much better prognosis than if the limb is analgesic. This gradation of functional loss gives the clinician a very useful indication of the severity of a lesion.

Nerve injuries

Nerve injuries can also be classified according to the functional integrity of the nerve.

Neurapraxia - compression, oedema and local demyelination can result in a complete block of impulse conduction in the nerve without loss of anatomical continuity.

This is termed a neurapraxic injury, which is the mildest form of injury. Recovery will usually occur within one to two weeks once the compression and oedema resolve. Local demyelination may take a little longer to reverse (about 4-6 weeks).

Axonotmesis - if the injury is more severe, axons may degenerate distal to the lesion, although their axon sheaths remain intact. This is termed axonotmesis. Recovery will now depend on regrowth of the axons from the site of injury, which normally occurs no faster than 1-2 mm per day (Uchida *et al* 1993).

Neurotmesis - the most severe type of injury is termed neurotmesis and occurs when there is loss not only of axonal continuity, but also of continuity of the whole nerve trunk. Recovery will then depend on the axonal regrowth successfully crossing the resultant neuroma to reach the axon cylinders on the distal side of the lesion. This often proves to be impossible, or at best regeneration is incomplete.

Electrophysiological evaluation

Three electrophysiological techniques may be of value in assessing the severity of a lesion (see Chapter 4). These are:

1. Spontaneous EMG activity will occur between 7-10 days after an injury severe enough to cause Wallerian degeneration of axons.
2. Immediately following an injury to a nerve, EMG can be used to determine if any motor function remains in the muscles innervated by that nerve. By inducing a withdrawal reflex (stimulating an area that the animal can definitely feel) and simultaneously recording EMG activity from a flexor muscle, motor unit potentials will be recorded if any muscle function remains. For example, the presence of motor unit activity in the biceps brachii muscle of a dog with a brachial plexus injury implies that some functional axons must have survived through to the musculocutaneous nerve.
3. Motor and sensory nerve conduction studies, and the recorded amplitudes of muscle evoked action potentials, give the most accurate assessment of the severity of the damage to the LMN. A period of 7-10 days should pass before assessment.

Lesions in Specific Neuroanatomical Areas

Specific conditions that affect each of the four areas discussed under lesion localisation are now considered:

A: UMN lesions affecting cord segments C_1-C_5

Lesions at this level are unlikely to cause unilateral thoracic limb signs without involvement of the ipsilateral pelvic limb, and frequently deficits are also apparent on the contralateral side of the body. Spinal cord lesions affecting segments C_1-C_5, particularly intervertebral disc disease, can occasionally cause a monoparesis of one thoracic limb. This may be accompanied by Horner's syndrome.

B: LMN lesions affecting cord segments C_6-T_2

Spinal cord lesions in this region may cause a monoparesis, but are also highly likely to produce neurological deficits in other limbs. Potential causes include cervical vertebral instability, disc herniation, neoplasia, fibrocartilaginous embolism or discospondylitis. Horner's syndrome and loss of the panniculus reflex may occur. Localised tetanus could also suggest a lesion in this area (Malik *et al* 1989, see below).

C: Lesions of the brachial plexus or roots C_6-T_2

A lesion in this location should cause a LMN monoparesis without involvement of other limbs (unless the lesion has extended to involve the spinal cord). The main differentials are an avulsion injury, neoplasia, or inflammatory disease. Partial Horner's syndrome and loss of the panniculus reflex may also occur.

Two other rare conditions that could localise to this region are tetanus and vascular injury. Localised tetanus has been described as a cause of thoracic limb monoparesis, associated with muscle rigidity and spastic contraction of the affected limb (Malik *et al* 1989). Brachial artery injury has been described as a cause of ischaemia and monoparesis in one dog (McCoy and Trotter 1977).

Assessment of LMN thoracic limb monoparesis localising to this region is best considered under the following syndromes:

- Dysfunction of the cranial brachial plexus
- Dysfunction of the caudal brachial plexus
- Dysfunction of the complete brachial plexus
- Dysfunction of the radial nerve alone - see below

Cranial brachial plexus. Lesions in this location result in denervation over the suprascapular and musculocutaneous peripheral nerve fields. The usual causes are an avulsion injury to the roots of the cranial brachial plexus, or a tumour occupying the C_6 or C_7 nerve roots or the cranial portion of the common plexus bundle. The most important clinical sign will be loss of elbow flexion, evaluated either by attempting a thoracic limb placing response or by asking the dog to "shake hands". There may be an associated mild weakness of the radial nerve. Sensation in the limb distal to the elbow joint will be intact, except possibly for a small area on the medial antebrachium (Bailey and Kitchell 1987).

Caudal brachial plexus. Lesions here result in denervation over the radial, median and ulnar peripheral nerve fields. The usual causes are an avulsion injury to the roots of the caudal brachial plexus, or a tumour occupying the C_7,C_8 or T_1 nerve roots, or the caudal portion of the common plexus bundle. Clinically the animal will show a marked thoracic

limb proprioceptive deficit, a "dropped" elbow and carpus, and inability to bear weight on the limb. Sensation to the limb distal to the elbow may be absent except for a small area on the medial aspect of the antebrachium. The panniculus reflex is often absent and the animal may demonstrate partial Horner's syndrome.

Complete brachial plexus. Lesions of the entire plexus cause a combination of the previous two syndromes, with resultant paralysis over all peripheral nerve fields. A large neoplasm or complete avulsion of all nerve roots to the brachial plexus are the main causes of this syndrome. The animal is unable to flex the elbow joint or bear any weight on the limb. Analgesia, if present, is usually complete distal to the elbow joint and may extend proximally. A loss of the ipsilateral panniculus reflex and / or a partial Horner's syndrome will often be seen.

D: Lesions affecting the radial nerve

In one study, six per cent of humeral fractures in dogs had associated radial nerve palsy, but all recovered within five months (Vannini *et al* 1988). In radial nerve injury, there is an inability to fix the elbow and carpal joints, a "dropped" elbow, knuckled-over carpus, and selective sensory denervation to the cranial antebrachium. If the lesion is distal to the branch supplying the triceps muscle, then elbow extension will be preserved. There is neither Horner's syndrome nor loss of the panniculus reflex.

Avulsion of the Nerve Roots of the Brachial Plexus

This is by far the most common thoracic limb nerve injury encountered in small animals (Griffiths *et al* 1974). It is frequently referred to simply as "brachial plexus avulsion".

Avulsion of the nerve roots is a more accurate term, as the traction injury nearly always causes damage at the origin of the nerve roots from the spinal cord, and not at a more peripheral portion of the plexus. The nerve roots are mechanically the weakest structures between the spinal cord and the rest of the limb, as they lack a well defined perineurium, which is one of the three main connective tissue components of peripheral nervous tissue. The ventral (motor) roots appear to be more susceptible to rupture than the dorsal roots (Griffiths 1974).

The traction injury is the result of severe trauma, and in dogs and cats this usually occurs during a road traffic accident (RTA), or occasionally when an animal is hung by its foot in a fence. Every RTA patient should be screened for the existence of this injury. The presence of a root avulsion is often devastating in terms of the resulting paralysis, the complication of any co-existing orthopaedic repairs, the prolonged nursing care, and the poor overall prognosis.

Although the clinical signs are variable, nearly all cases can be divided into one of the categories described earlier.

Cranial plexus dysfunction

Injury to C_6 and C_7 nerve roots is probably caused by traction on the limb in a caudal direction. This injury is not commonly recognised as it only results in loss of shoulder movement and elbow flexion. Hemiplegia of the diaphragm (phrenic nerve, C_5) may also be demonstrable using fluoroscopy.

Caudal plexus dysfunction

Injury to C_7 or C_8 - T_2 nerve roots is probably caused by traction on the limb in a cranial direction. This accounts for roughly one third of documented cases (Griffiths 1977).

Complete plexus dysfunction

Injury to nerve roots C_6-T_2 probably results from severe traction or possibly abduction of the limb. It is the most common presentation and causes the most profound deficits.

Caudal and complete plexal injuries are particularly devastating. Preservation of any ability to flex the limb (so that the foot is carried off the ground) considerably reduces the complications associated with digital excoriation.

Diagnosis

It is important to screen all animals that cannot use their thoracic limb(s) following trauma for a possible avulsion injury, particularly those that are recumbent or have orthopaedic injuries. Screening can be performed very quickly by checking for Horner's syndrome and loss of the panniculus reflex. Approximately 70% of patients with brachial plexus root avulsions have one or both of these abnormalities (Wheeler *et al* 1986). The withdrawal reflex and deep pain sensation in the lateral digit may also be absent. For a few weeks after an avulsion injury, the affected limb may also be much hotter (10°C) than the others, due to loss of sympathetic vascular tone.

Further diagnostic procedures should include electrophysiological techniques if possible. The use of EMG to confirm a diagnosis is very useful if performed 7-10 days after injury. Serial nerve conduction studies of the radial nerve can provide valuable prognostic information (Steinberg 1979).

Pathology

The lesion occurs predominantly inside the dura mater, at the junction of the spinal cord and the nerve roots. Usually there will be a complete loss of continuity in the most severely affected roots, while adjacent roots may be only partially avulsed. The torn roots often end up attached as a fibrous mass to the first rib (Griffiths 1974).

Management

This condition is, unfortunately, not amenable to any form of therapy directed at the avulsion itself. The final outcome depends on the degree of permanent damage sustained at the time of injury. Oedema and demyelination of nerve roots will resolve over 1-2 months. In animals that show no improvement over this period, or in which excoriation of the digits or carpus occurs, amputation is often the best solution.

Tendon relocation is one surgical option to lessen the effects of the injury. Two approaches are available, directed at providing extension of the elbow and carpus respectively (Bennett and Vaughan 1976). Although these techniques can work well in selected patients, it is essential that the muscle to be relocated has normal function in order to take on its new role. This must be determined by EMG and NCV examination.

Carpal arthrodesis is an alternative to prevent the carpus from collapsing. One disadvantage with this procedure is that the digits remain paralysed, so weight bearing on the digital pads is uneven and may result in excessive wear. In addition, the limb will usually remain analgesic and so cannot benefit from the normal protective reflexes.

Proper client education is essential in avulsion injuries to stress the fact that surgery is only an attempt to salvage function from a paralysed limb. If it does not work, amputation may still prove necessary. During the first two months, while any reversible component to the nerve injury is recovering, strict attention to hygiene, prompt attention to wounds, protection of the foot by a leather or wire mesh boot, and physical therapy to keep joints and muscles mobile, are all crucial. This calls for a large time commitment on the part of the owner, and good compliance from the animal. Therefore, strict case selection is crucial. If the animal can carry the limb in flexion, then the major complication of carpal and digital abrasions can be avoided.

Prognosis

This is often quite favourable with cranial plexal avulsions because the animal can still bear weight on the limb, and the normal pain sensation renders excoriation of the digits unlikely.

The prognosis is generally very poor following complete avulsion. Rare animals are seen with a complete plexal injury, which make a full recovery within one or two weeks. It is presumed that the injury in such cases is purely neurapraxic with no loss of continuity of the nerve roots. Most animals, however, show no improvement.

The prognosis is similarly disappointing for most cases with a caudal plexal deficit. Animals that show preservation of elbow flexion are easier to manage, and the very few cases with some ability to bear weight on the limb obviously have a much better prognosis.

The presence of normal deep pain sensation over the limb suggests sparing of the dorsal roots, which may correlate with a less severe injury to the ventral roots. In general, if no improvement has taken place within one or two months, useful functional recovery is unlikely.

Complications

Long term disuse of a limb can have several sequelae such as:

Contracture of joints due to muscle fibrosis or abrasion of the foot. The abrasion may become so severe as to erode portions of the digits, set up an osteomyelitis in the phalangeal bones, and introduce infection into tendon sheaths, which will then further exacerbate the contractures.

Trophic ulcers are the result of ulceration of denervated pads (Read 1986). The denervated skin is less resistant to the pressure of weight bearing, has poor vascular tone, may contact the ground at an unusual angle, and cannot be protected by normal reflexes. Trophic ulcers may occur following carpal or hock arthrodesis for the same reasons and can therefore invalidate any corrective procedures. These ulcers can be very difficult to deal with, although surgical techniques are described, which involve transfer of normally innervated skin into the affected area.

Paraesthesias can be an unfortunate complication during the management of any neurological patient. They may have a delayed onset as a result of nerve entrapment or reinnervation, and have been described in up to 15% of animals with neurological deficits resulting from pelvic fractures. Similar figures are not available for brachial plexus lesions. The resultant self mutilation considerably complicates case management.

Limb amputation is often the most practical course of action with severe injuries. Animals with major orthopaedic problems or severe arthritis in another limb are poor candidates for amputation and euthanasia may then be a consideration.

Neoplasia of the Brachial Plexus and Associated Nerve Roots

Primary tumours in this region may be neural or non-neural in origin. Neural tumours can be referred to under the general term nerve sheath tumour, but are also subdivided into Schwannomas, neurofibromas, neurolemmomas and neuromas. The terms malignant Schwannoma or neurofibrosarcoma are the most applicable for use in animals, as these tumours are nearly always malignant. (Figure 11.2). Tumours in this re-

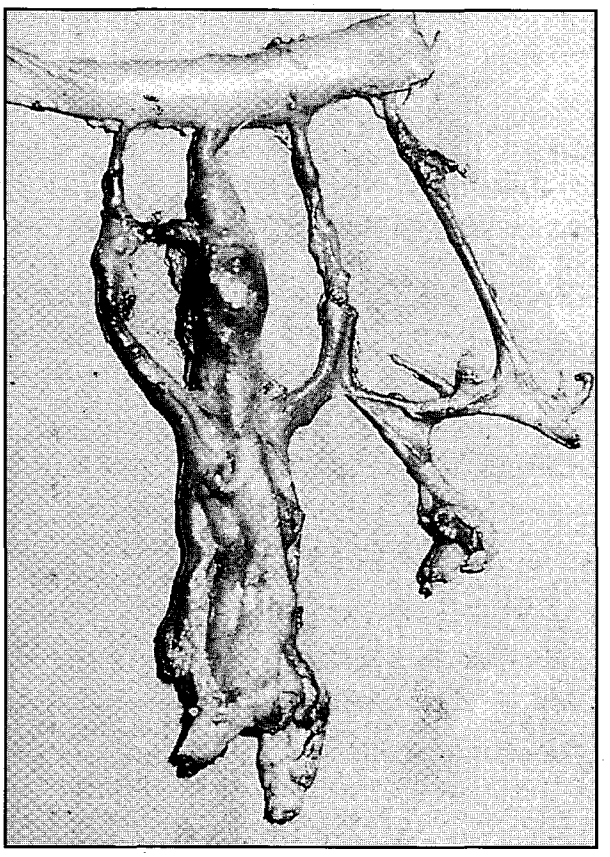


Figure 11.2: Typical appearance of a brachial plexus nerve sheath tumour in a dog (Courtesy of Dr. S. J. Wheeler).

gion can also be non-neural and simply compress or invade the plexus. These tend to be larger than primary neural tumours and so may be more easily detected. Examples would include osteosarcomas and chondrosarcomas (Griffiths and Carmichael 1981).

Of the reported tumours affecting the brachial plexus in dogs, about 50% showed evidence of spinal cord compression or invasion. In a few dogs the tumour appears to arise primarily in a dorsal nerve root, and therefore is situated predominantly or completely within the vertebral canal. The majority appear to arise peripherally and only invade the spinal cord as a terminal event. This situation is the reverse of that occurring in the lumbosacral plexus, where the majority of tumours appear to arise within the vertebral canal (Bradley *et al* 1982).

Medium or large breed dogs over seven years of age are most frequently affected. All initially demonstrate a thoracic limb lameness or paresis, which in some dogs progresses to involve one or more of the remaining limbs. Classically, dogs show a chronic intractable thoracic limb lameness for 6-8 months prior to presentation (Wheeler *et al* 1986).

Clinical features

It can be seen from Table 11.2 that marked muscle atrophy of the involved limb is the most useful diagnostic feature, together with the history of chronic lameness or paresis. The neurogenic nature of the muscle atrophy can be confirmed by EMG. Most animals show evidence of a LMN-type deficit, but about 25 % of patients only show lameness and demonstrate no neurological deficit in the affected limb.

Another useful features is the presence of a palpable mass in the axilla. This may be small, firm and cord-like or it may be large. In some animals, no mass is palpable but hyperaesthesia is evident on palpation of the axilla. In some dogs this hyperaesthesia is hard to localise, and may suggest a cervical or thoracolumbar lesion.

Ipsilateral loss of the panniculus response, and partial or complete Horner's syndrome may be present.

Radiography

Survey radiography is unrewarding in most cases, although oblique views of the spine may reveal enlargement of an affected intervertebral foramen by pressure atrophy. Myelography often reveals a higher incidence of spinal cord involvement than was apparent from the neurological examination. In one series, only half of the affected dogs with positive myelographic findings showed pelvic limb neurological deficits. This would suggest that myelography be performed in all cases if the full extent of the tumour is to be appreciated. The classic radiological appearance of a nerve sheath tumour that has extended to an intradural location is of an intradural - extramedullary lesion (see Chapter 5). Computed tomography may also be useful to identify brachial plexus tumours. Chest metastasis is rare but thoracic radiographs should be taken.

Treatment

In dogs with spinal cord involvement, a dorsal laminectomy is recommended to confirm the diagnosis and determine if removal is possible. Nerve sheath tu-

Table 11.2: Clinical features of brachial plexus tumours based on 27 reported cases.

Feature	Percentage
Limb muscle atrophy	88
Axillary mass	69
Axillary hyperaesthesia	60
Panniculus loss	54
Horner's syndrome	29

mours are usually slow growing, but it is often exceedingly difficult to determine the margins of neoplastic tissue. If the peripheral extent of the mass within the associated spinal nerve is not visible at laminectomy, successful removal of an intradural mass should be followed by exploration of the spinal nerves and brachial plexus, usually via a separate approach.

Two surgical approaches to the canine brachial plexus have been described. The craniomedial approach through the axilla gives good exposure of the common brachial plexus bundle and the major peripheral nerves (Knecht and Green 1977). The craniolateral approach gives good exposure to the more proximal portion of the common plexus bundle and the ventral branches of the spinal nerves C_6-T_1 (Sharp 1988). The initial choice depends on the location of the mass; the two techniques can be combined if necessary. Grossly involved tissue is normally non-functional so may be biopsied with minimal effect. Less obvious cases should undergo careful fascicular biopsy (Braund *et al* 1979). Following exploration and biopsy, the neurological deficit may be more pronounced. Following definitive diagnosis, it is most common to amputate the forequarter and remove spinal nerves C_6-T_2 as far proximal as is feasible. Nerve sheath tumours have very diffuse and ill-defined borders and are very prone to recurrence. This radical approach is preferred to give the dog the best chance of long term remission or cure. Local resection of the neoplastic portions of the plexus will usually leave the animal with a severe neurological deficit and also has a strong tendency towards early recurrence. The suitability of the candidate for forequarter amputation should be considered with respect to arthritis in the pelvic limbs or contralateral thoracic limb. Despite using an aggressive approach and postoperative radiotherapy, results have been very disappointing.

Prognosis

These tumours are very locally invasive, although evidence of local or distant metastasis is not common. Nerve sheath tumours are difficult to remove completely, because the exact extent of the neoplasm may be very difficult to discern on gross examination of the nerves. The prognosis for non-neural tumours is generally poor, as most are sarcomas with high invasive and metastatic potential.

Summary

A high index of suspicion should be observed in a middle aged or older dog with chronic intractable thoracic limb lameness and poorly localised pain, particularly if any neurological deficit is present. Rapid institution of diagnostic procedures such as electromyography and myelography will be needed for diagnosis, with early exploratory surgery as a further diagnostic tool. Once confirmed, amputation with removal of all involved spinal nerves as far proximally as possible offers the best long term prognosis. Nerve sheath tumours do not appear to be particularly radiosensitive.

Feline brachial plexus tumours

Only four such cases have been recorded, one due to a chondrosarcoma, two lymphosarcoma, and one due to reticulosis (Shell and Sponenberg 1987; Spodnick *et al* 1992). The prognosis is even worse than in the dog due to the high potential for involvement of other body regions, which occurred in each of these cats. The clinical features were similar to those in the dog, although affected cats tend to be younger.

Brachial Plexus Neuritis

Only two cases have been reported in the dog (Alexander *et al* 1974). Although both dogs showed bilateral involvement, cases in humans are often unilateral. The aetiology is not known, but in humans some cases follow administration of vaccines, sera or other foreign proteins and the neuropathy is preceded by malaise, vomiting and urticaria. One dog demonstrated these signs and the cause was confirmed to be a horse meat diet; in the second the cause was not found and there was no preceding illness. The prognosis is good in humans but full recovery usually takes months or even years. One dog could not walk and was destroyed, the second remained ambulatory but showed only minimal improvement over four months. A dog with brachial plexus neuritis is shown in Figure 11.3. Affected dogs may respond to corticosteroids and a change to a poultry based (hypoallergenic) diet (Steinberg 1988).

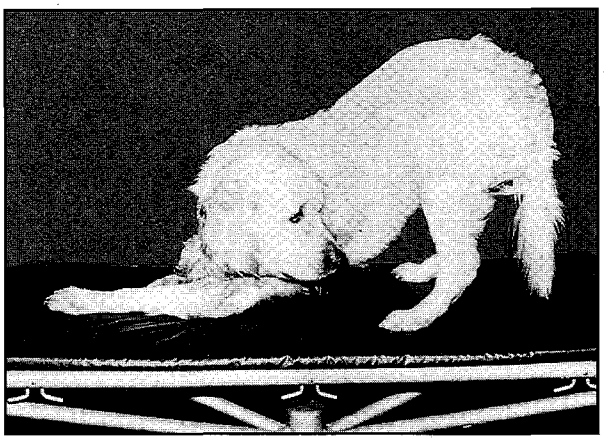


Figure 11.3: *Dog with chronic bilateral brachial plexus neuritis and associated thoracic limb weakness (Courtesy Dr. S. J. Wheeler).*

PELVIC LIMB

Anatomy of the Lumbosacral Plexus and Pelvic Limb Innervation

The lumbosacral plexus is derived largely from spinal cord segments L_4-S_2. Due to the disparity in lengths of the spinal cord and the vertebral column, the last three lumbar segments reside over the fourth lumbar verte-

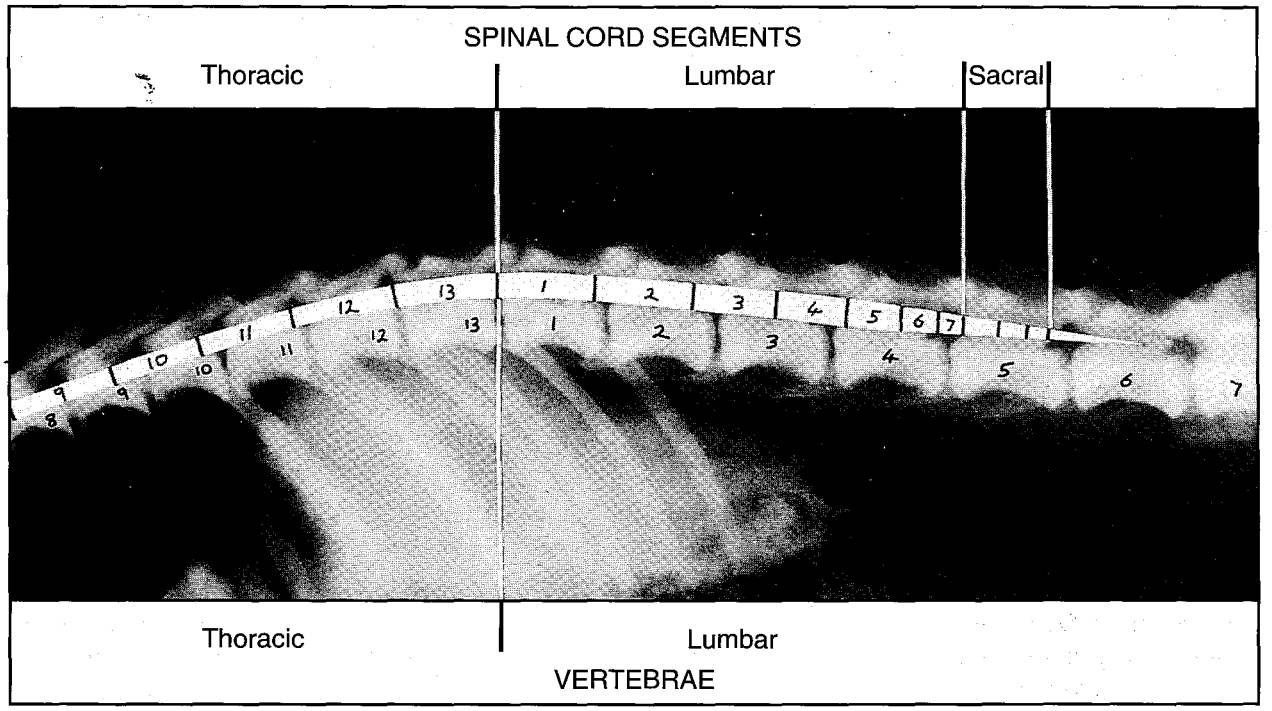


Figure 11.4: *Diagram to show the relative positions of spinal cord segments and vertebral bodies (From Wheeler, S. J. (1985) The approach to spinal disease in dogs* British Veterinary Journal ***141****, 222, reproduced by permission).*

bra and the three sacral segments lie over the fifth lumbar vertebra (Figure 11.4). In the cat and sometimes in small breeds of dogs, the three sacral segments may reside over the $L_{5/6}$ disc or even partly over the L_6 vertebral body.

If we remember the order (from cranial to caudal) in which the four main peripheral nerves to the pelvic limb and pelvic region arise:-

Femoral - Obturator - Sciatic - Pudendal

then it is logical that an approximation of their nerve roots of origin is as follows (see Figure 11.5):-

Femoral	Obturator	Sciatic	Pudendal
$L_{(4),5}$	$L_{(5),6}$	$L_{(6),7}$,S_1	$S_{1,2,(3)}$

This estimation is reasonable, as there is some degree of variation from animal to animal. As can be seen, each spinal cord segment usually contributes to more than one peripheral nerve.

Nerves of the pelvic limb

To consider each peripheral nerve individually (see Figure 11.5):

Femoral nerve - arises from the most cranial portion of the plexus, and innervates the most cranial muscle mass in the pelvic limb - the quadriceps group (Figure 11.5). This group of muscles extend the stifle joint and, together with the psoas muscle group, which is also innervated by the femoral nerve flex the hip joint. The saphenous branch of the femoral nerve supplies sensation to the medial aspect of the limb, usually as far as the first digit (dew claw), but sometimes as far as the medial aspect of the second digit. The autonomous test site for the femoral nerve is located just distal to the femoral epicondyle (Bailey and Kitchell 1987).

Obturator nerve - is a purely motor nerve which supplies the adductor muscle group, comprising the adductor magnus, pectineus and gracilis muscles (Figure 11.5).

Sciatic nerve - The intra-pelvic portion of the sciatic nerve is termed the lumbosacral trunk (Figure 11.6). The cranial and caudal gluteal nerves arise from this trunk before it exits the pelvis at the greater sciatic notch to become the sciatic nerve.

The sciatic nerve innervates the most caudally-situated muscle group on the thigh - the hamstring group. This muscle group serves to flex the stifle joint and, together with the gluteal group, which is innervated by the gluteal nerves, to extend the hip joint (Figure 11.5). At the level of the stifle the sciatic nerve divides into peroneal and tibial branches:

Peroneal nerve is the cranial branch, which innervates the skin and the muscle groups on the craniolateral surface of the tibia and foot. It therefore activates the hock flexor muscle group and the digital extensors. The autonomous zone is on the dorsal aspect of the digits.

Tibial nerve branches caudally and innervates the skin and the muscle groups on the caudal aspect of the tibia

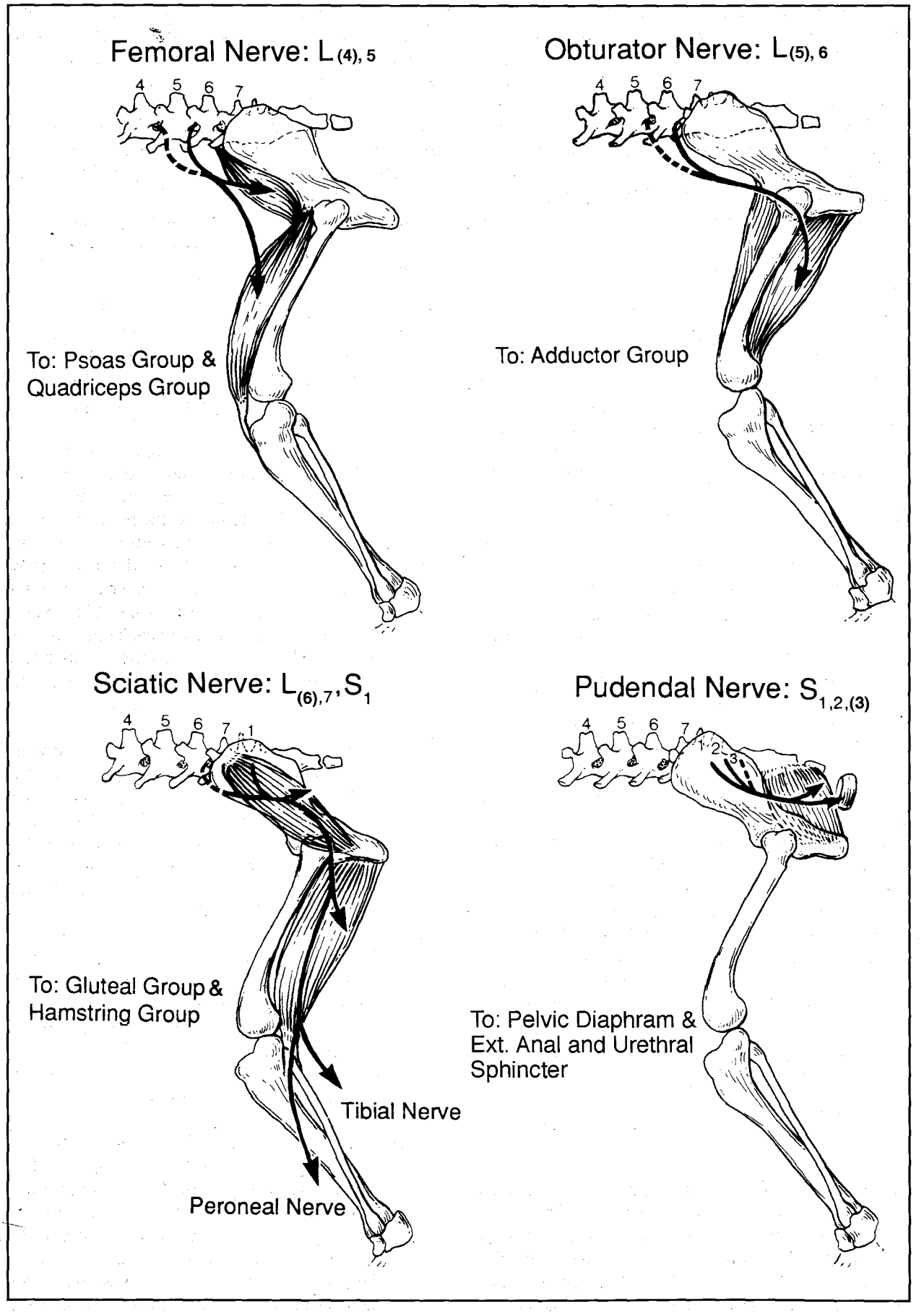


Figure 11.5: Diagram to show the main peripheral nerves arising from the lumbosacral plexus.

and foot. It therefore activates the hock extensor and the digital flexor muscle groups. The autonomous zone is over the metatarsal pad.

Pudendal nerve - is the most caudally-derived of the major branches of the lumbosacral plexus. It does not innervate any major limb muscles. Branches are motor to the muscles of the pelvic diaphragm, and the external anal and urethral sphincters (Figure 11.5). It is also sensory to the skin of the anus, perineum and genitalia.

Sacral and pelvic nerves - arise independently from the caudal part of the plexus (S_{1-3}) and supply autonomic innervation (including sensory function) to the pelvic viscera. They innervate the detrusor muscle of the bladder and contribute to normal urinary and faecal continence.

Caudal nerves - arise from the most caudal portion of the cauda equina and supply innervation to the tail. (These were known formerly as the coccygeal nerves.)

Neurological Examination

In any animal with a suspected neurological problem, the clinician must not omit to conduct a thorough assessment of the musculoskeletal system so that, for example, a cruciate ligament rupture is not missed. Similarly, any dog presenting with an orthopaedic lesion, particularly following trauma, must have an assessment of its neurological status. Over 10% of dogs and cats with pelvic fractures or fracture / dislocations have associated neurological deficits.

The neurological examination should first determine whether the deficit is UMN or LMN in character (see Chapter 3). The most sensitive indicator of mild LMN disease in the pelvic limb is usually a weakness in hock flexion. This should be compared with the normal limb or to a control animal. Marked muscle atrophy will usually develop in the affected limb; its exact distribution can be used to further characterise the LMN deficit using the anatomical knowledge obtained from Figure 11.5. The severity of the neurological deficit can be assessed as described above.

Clinically, LMN disease can produce four relatively distinct syndromes, which may occur in isolation or in various combinations (see Table 11.3):

- Femoral-type deficits
- Sciatic-type deficits
- Sacral deficits
- Caudal deficits

Femoral-type deficits - lesions may be due to damage at either L_4 or L_5 spinal cord segments, their nerve roots or spinal nerves, or by damage to the femoral nerve itself. Of the four types of LMN syndrome, the femoral nerve deficit is the least commonly encountered, partly because the nerve and the spinal nerves contributing to it are very well protected within the sublumbar musculature. The L_4 or L_5 spinal cord segments and nerve roots within the vertebral canal are more likely to be affected, mainly by trauma or neoplasia.

A lesion in this location is therefore very likely to cause signs in the contralateral limb. Femoral-type deficits cause severe gait dysfunction, due to an inability to fix and bear weight on the stifle joint. Hip flexion is also markedly reduced. Analgesia or hypalgesia may occur over the medial aspect of the thigh, crus, metatarsus and first digit. The patellar reflex will usually be reduced or absent.

Sciatic-type deficit - damage to either L_6-S_1 spinal cord segments, their nerve roots or spinal nerves, the intra-pelvic lumbosacral trunk, or the sciatic nerve itself (see Figure 11.6) can present as sciatic neuropathies. These can be subdivided into four types:

1. Lesions at, or proximal to, the lumbosacral trunk cause complete sciatic-type deficits. They result in an inability to extend the hip, flex the stifle, or to flex or extend the hock. The digits are also paralysed. Even with such profound deficits the animal can still fix the stifle (via the femoral nerve) and can often bear some weight on the limb. The foot usually knuckles and the hock collapses. Analgesia may be present over the whole limb distal to the stifle, except on the medial aspect (which is supplied by the saphenous branch of the femoral nerve).

2. Lesions of the sciatic nerve itself (i.e. between the greater sciatic notch of the pelvis and the stifle joint) usually preserve gluteal muscle function. If the lesion is distal to the greater trochanter of the femur, then the hamstring muscles are also spared, so that the animal can still flex its stifle but is paralysed below the level of the stifle joint itself.

3. Pure tibial nerve lesions are rare. The main features will be loss of hock extension so that the animal walks in a plantigrade manner. Analgesia, if present, will occur on the caudal aspect of the limb distal to the stifle. Tibial nerve function may be selectively disturbed (usually bilaterally) in feline diabetic neuropathy.

4. Peroneal nerve lesions are seen much more commonly than tibial deficits. The main features are weak hock flexion, possibly combined with reduced sensation of the cranial crus and foot. Injuries to the lumbosacral trunk or the sciatic nerve in humans cause dysfunction of the peroneal nerve up to six times more often than the tibial nerve; this also seems to hold true for animals.

It is relatively easy to detect a sciatic neuropathy in an animal that can walk, as conscious proprioceptive deficits and paresis of appropriate muscle groups are visible. However, to diagnose a moderate sciatic neuropathy in a dog with severe pelvic fractures is very important and often much more difficult.

The first useful diagnostic feature is the inability of an animal with sciatic motor deficits to actively flex the hock joint. The withdrawal reflex is mediated through the sciatic nerve, except for some hip flexion (psoas muscle) and weak stifle flexion (sartorius muscle), which are mediated by the femoral nerve. Hock flexion is, however, mediated solely by the peroneal division of the sciatic nerve. This is evaluated by applying a painful stimulus to the digits while also gently extending the hock. Most neurologically-intact animals with pelvic fractures can firmly flex the hock joint against moderate resistance, particularly if this does not involve movement of the whole limb. If in doubt, the opposite limb should be evaluated or a control dog assessed. If analgesia or hypalgesia over the sciatic field is suspected, then the sensory field of the femoral nerve should be stimulated. The most sensitive means of detecting reflex contraction of the hock flexor muscles is by the use of an EMG needle to detect motor unit potentials.

A second assessment depends on the conscious response to a painful stimulus, caused preferably by using haemostats on the nail-bed. This should be compared to the other pelvic limb and to one or both thoracic limbs. Most neurologically-intact animals with pelvic fractures are well able to respond consciously to such a stimulus even if they are somewhat reluctant to move the limb. If hypalgesia is suspected, the animal's response to a similar stimulus on the dew claw (first digit) and medial metatarsus should be normal, provided that the femoral pathways are intact.

An inability to flex the hock joint and selective loss of sensation over the sciatic field should arouse a high index of suspicion for sciatic nerve dysfunction. Early recognition may have a considerable bearing on the overall case management. For prognosis, see the section on Assessing the severity of a lesion above.

Sacral deficit - this is a general term used for deficits of either the sacral spinal cord segments, their nerve roots or spinal nerves, or of the pudendal, pelvic or sacral nerves themselves. These structures together innervate the muscles within the pelvis, supply sensation to the perineal region, and are important for control of continence (see Chapter 12). The anal reflex and the function of both the external urethral sphincter and detrusor muscles are good indicators of the integrity of this region. The external anal and urethral sphincters are mainly controlled through S_1, while S_2 is important for detrusor function.

Caudal deficit - injury to the caudal spinal cord segments or nerves will produce a combination of motor and sensory disturbance to the tail.

Lesions in Specific Neuroanatomical Areas

Having characterised the deficit to one of the above four types by neurological examination, the clinician should now be able to localise the lesion as described in Table 11.3 and illustrated in Figure 11.6.

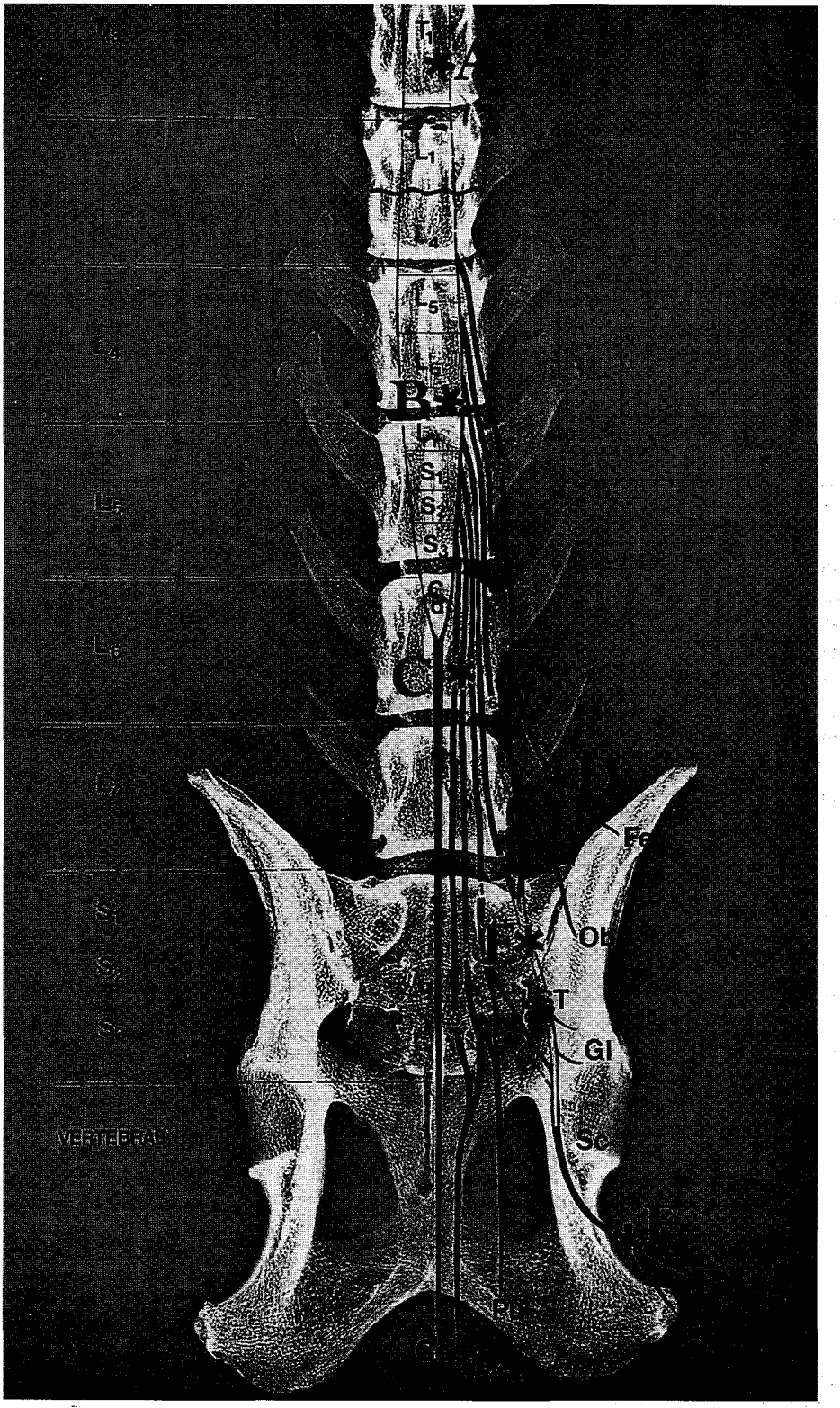
A: UMN lesions affecting cord segments T_3-L_3

In UMN lesions, the spinal reflexes should be normal or hyperactive. Because it is unusual to selectively damage one half of the spinal cord, lesions at this level nearly always affect both pelvic limbs and so usually cause bilateral proprioceptive deficits. Occasionally, an animal may present with almost completely unilateral signs in the limb ipsilateral to the spinal cord lesion. It may then require careful sequential neurological examination, or evaluation of the initial signs of the disease, to detect evidence of contralateral limb dysfunction.

Table 11.3: *Classification scheme for lesion localisation. (The areas correspond to Figure 11.6).*

	LOCALIZATION	DEFICIT
A:	T_3-L_3 SPINAL CORD	UMN
B:	L_4-S_3 SPINAL CORD	LMN, F, Sc, Sa, or Ca
C:	L_4- CAUDAL NERVE ROOTS	LMN, F, Sc, Sa, or Ca
D:	FEMORAL NERVE	LMN, F
E:	L_6-S_1 SPINAL NERVES AND LUMBOSACRAL TRUNK	LMN, Sc, (Sa)
F:	SCIATIC NERVE	LMN, Sc

LMN = Lower motor neuron deficit
UMN = Upper motor neuron deficit
F = Femoral-type deficit
Sc = Sciatic-type deficit
Sa = Sacral deficit
Ca = Caudal deficit



Fe - Femoral nerve
Ob - Obturator nerve
Gl - Gluteal nerves
H - Nerve to hamstring muscles)
T - Tibial nerve) = *Sc*
P - Peroneal nerve)
Sc - Sciatic nerve)

LST - Lumbosacral trunk
Pu - Pudendal nerve
Pe - Pelvic nerves
Sa - Sacral nerves
Co - Caudal nerves

Figure 11.6: *Diagram to show the six possible sites of injury that may result in hindlimb monoparesis/monoplegia. (see Table 11.2).*

The following UMN lesions may cause a pelvic limb monoparesis:-

Ischaemic myelopathy - a unilateral infarct will often leave the animal with a neurological deficit largely restricted to the ipsilateral pelvic limb, once the early oedematous change in the contralateral spinal cord has resolved. Pain sensation to the affected limb is usually preserved (due to cross over of nociceptive fibres in the spinal cord distal to the infarction). Lesions in the T_3-L_3 area usually have a better prognosis than those occurring in the lumbosacral enlargement (area B, below), where the crucial ventral horn cells of the LMNs are located.

Intervertebral disc disease - cases with almost complete lateralisation may be encountered. The likely breed incidence, focal thoracolumbar hyperaesthesia, and the myelographic demonstration of an extradural lesion should confirm the diagnosis.

Neoplasia - a gradual progression of the neurological deficit, and frequently also the presence of spinal hyperaesthesia, are the main presenting signs. Bone lysis on survey radiography or myelographic demonstration of a lesion should confirm the diagnosis.

B: LMN lesions affecting cord segments L_4-S_3

As shown in Figure 11.4, these six spinal cord segments overlie vertebral bodies L_3, L_4, and L_5. Even unilateral lesions affecting spinal cord segments L_4-S_3 are highly likely to result in bilateral conscious proprioceptive deficits or diminished spinal reflexes, and frequently also produce sacral deficits. In addition, there may be sensory loss to both the affected pelvic limb(s) and perineum. Severe damage to this region of the spinal cord usually has a bleak prognosis because the LMNs cannot be replaced.

The most common LMN spinal cord lesions causing pelvic limb monoparesis are:-

Intervertebral disc disease - approximately 10% of disc herniations occur between discs $L_{3/4}$ and $L_{5/6}$ inclusive. From Figure 11.4, it can be seen that these affect spinal cord segments L_4-S_3. Marked lateralisation of signs is sometimes seen.

Degenerative myelopathy - early signs in this condition are often markedly lateralised. Involvement of dorsal nerve roots in up to 40% of cases is clinically associated with depression of the patellar reflex. This can cause the clinician to localise the lesion to the L_4-S_3 spinal cord.

Ischaemic myelopathy - see above.

Neoplasia - see above.

Localised tetanus - this has been described as a cause of thoracic limb monoparesis, associated with muscle rigidity and spastic contraction of the affected limb (Malik *et al* 1989). This could also occur following a wound in the pelvic limb.

C: Lesions of nerve roots L_4-Ca

The nerve roots of the cauda equina lie caudal to the $L_{5/6}$ intervertebral space. Lesions occurring at this level of the nervous system will obviously cause clinical signs very similar to those at B, as can be seen from Table 11.2. Survey radiographs, myelography, epidurography and in some cases CSF analysis should help to differentiate spinal cord lesions from nerve root lesions.

Fracture of L_6 and L_7 vertebral bodies - only nerve roots (and not spinal cord) overlie the L_6 and L_7 regions of the vertebral canal. Nerve roots are better able to tolerate displacement than is the spinal cord. Even a severely displaced fracture at this level may cause surprisingly few deficits. Occasionally a monoparesis or monoplegia will be seen, often combined with peroneal weakness. Of the L_7 vertebral body fractures reported in dogs, almost half presented with only pain and reluctance to walk. These dogs returned to normal within six weeks without surgical intervention. Dogs with more severe clinical signs showed sciatic-type deficits, in most cases combined with urinary and faecal incontinence (Slocum and Rudy 1975). Following either surgical or conservative therapy, a proportion of cases may be left with permanent deficits, usually referable to either the peroneal nerve or a disturbance of continence.

Fracture / luxations of the sacrocaudal area - animals with fractures or luxations in the sacral or caudal area often present with weakness or lameness in one or both pelvic limbs. This usually occurs due to an associated traction injury to the more proximal nerve roots of the cauda equina. The pelvic limb neurological deficits are usually mild and improve within one week of the injury.

The severity of the sacral and caudal neurological deficits can be used as a guide to prognosis. In a review of over fifty cats with this injury (Moise and Flanders 1983; Smeak and Olmstead 1985):

- Cats with only caudal nerve (tail) deficits had a 100% recovery rate.
- Cats with urinary retention in addition to caudal nerve deficits had a 75% recovery rate.
- Cats showing caudal nerve deficits and urinary retention, together with decreased anal tone or perineal sensation, had only a 60% recovery rate.

- Cats with caudal nerve deficits, urinary retention, decreased anal tone and perineal sensation combined with a lack of urethral sphincter tone (as assessed by ease of bladder expression) had the worst prognosis, with only 50% recovering.
- The most important information from this series was that all cats that did not recover the ability to urinate normally within one month of the injury remained incontinent.

Although tail amputation has been advocated to prevent further traction on the cauda equina, it did not affect the overall recovery rate. It may be of benefit to prevent soiling or accidental trauma to the tail.

Neoplasia of nerve roots L_4-S_3 - tumours arising from the lumbosacral nerve roots or plexus have been described with much less frequency than tumours in the brachial plexus region (Bradley *et al* 1982). Signs of contralateral limb dysfunction appear early, as most lumbosacral tumours are located intradurally, whereas intradural invasion is usually a delayed event with tumours of the brachial plexus.

Lumbosacral spondylopathy - clinical signs do vary considerably and although weakness is usually bilateral, a unilateral sciatic-type neuropathy is not unusual. Weak hock flexion was recorded as the main neurological deficit in one series (Denny *et al* 1982). EMG is useful to confirm that the neurological deficits are referable to the lumbosacral plexus.

Intervertebral disc herniation - lesions here are considered as part of the lumbosacral spondylopathy / cauda equina syndrome. Pelvic limb lameness was most often unilateral in the seven dogs with this condition recorded by Denny *et al* (1982).

Discospondylitis - dogs with LS discospondylitis may show pain and lameness of one pelvic limb, together with muscle atrophy and EMG evidence of denervation.

Inflammation of the cauda equina - this may result from infectious processes such as distemper, toxoplasmosis, neosporosis, or FIP, and can also be a feature of Coonhound paralysis. Signs may be initially either unilateral or bilateral. Toxoplasmosis and neosporosis may cause extension of the pelvic limbs in young animals. A polyradiculoneuritis of unknown aetiology analogous to cauda equina neuritis in horses, has been described in two dogs, one of which had unilateral onset of signs (Griffiths *et al* 1983).

Feline aortic emboli - although not primarily a neural lesion, the resultant ischaemia causes a peripheral neuropathy, which is superimposed on the more obvious ischaemic myopathy. The clinical signs and pulse deficit may be more marked in one pelvic limb, but paraparesis or paraplegia is nearly always seen with this condition (See Chapter 15).

D: Injury to the main trunk of the femoral nerve

Injuries to this structure are very rare. They may occur following prolonged caudal limb extension over the edge of an operating table, such as during perineal hernia surgery. Masses in the region of the psoas muscles may also cause femoral-type deficits.

E: Injuries to the ventral branches of L_6, L_7 and S_1 spinal nerves or to the lumbosacral trunk

These neural structures are very close to the pelvis and are the most important sites for serious nerve injury in the lumbosacral plexus. Of 474 fractures or luxations occurring in dogs and cats, 26% involved the pelvis (Kolata and Johnston 1975). In a retrospective survey of pelvic fractures or luxations occurring over a 4.5 year period, 35 dogs and cats (reflecting 11% of the total number of animals seen) had associated neurological deficits (Jacobsen and Schrader 1987). A similar incidence has been reported for feline pelvic fractures (Bookbinder and Flanders 1992).

Pelvic fractures

These can be classified as (Figure 11.7):

- **Type I** Comminuted
- **Type II** a. Segmental with two major fracture lines, one on either side of the acetabulum
  b. Fractures through the acetabulum
  c. "Open book" involving the pubic symphysis area, together with either a sacroiliac luxation or a longitudinal sacral fracture. The isolated hemipelvis is free to rotate (or open like a book, see inset Figure 11.7).
- **Type III** Stable

Type I and II fractures have the highest incidence of associated neural and soft tissue injuries. In a prospective survey over one year, 40% of Type II pelvic fractures in dogs and cats had concomitant neurological deficits. Half were "open book" (Type 11c) fractures involving the sacroiliac joint or sacral wing, and half were segmented ilial shaft (Type IIa) fractures (Sharp 1982). Of 34 canine pelvic fractures causing neurological deficits, nearly all occurred in association with sacroiliac luxations or segmental ilial shaft fractures (Jacobsen and Schrader 1987).

In general therefore, the following three types of pelvic fracture in the dog and cat have a very high incidence of sciatic type neurological deficits:

- sacroiliac luxations
- longitudinal sacral fractures (sacral wing)
- ilial shaft fractures

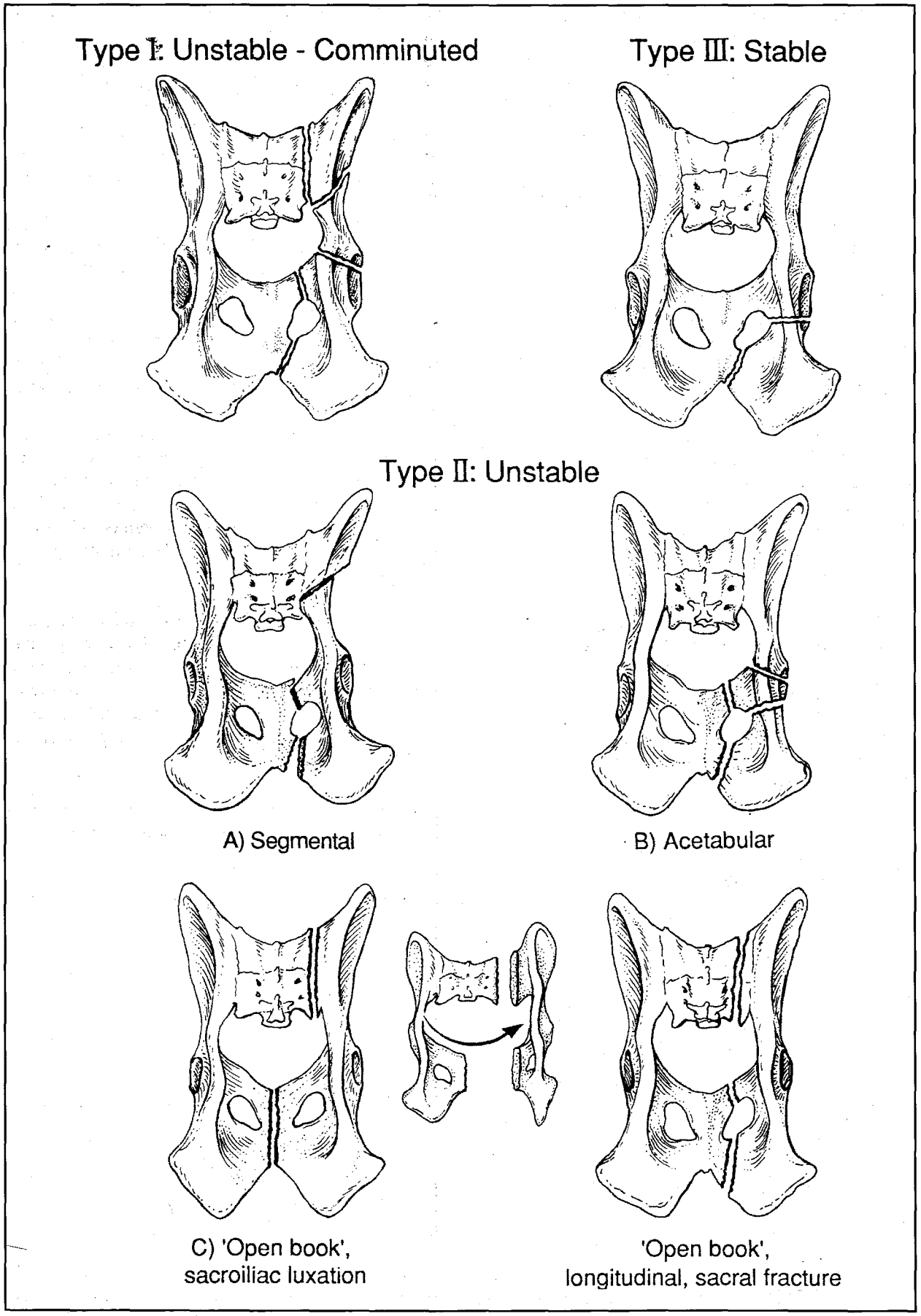


Figure 11.7: Diagrams to show the three main types of pelvic fracture.

Neural damage usually occurs either to the lumbosacral trunk or to the ventral branch of S_1 spinal nerve, both of which lie very close to these fracture sites and are only poorly protected by surrounding soft tissue. The resultant injury causes a neurological deficit that is clinically indistinguishable from an injury to the sciatic nerve itself. Some patients may also show mild sacral signs such as anal hyporeflexia, presumably due to injury to the S_1 ventral spinal nerve, which lies close to the lumbosacral trunk.

If the animal shows urinary retention, then it is likely that S_2 nerve root has also been damaged. This is most likely to occur in longitudinal sacral fractures (those occurring through the sacral foraminae). Other sacral signs may then be seen, including decreased anal tone, analgesia to the perineal area, as well as sciatic-type deficits.

Confirmation of an injury at this location of the lumbosacral plexus is obtained by EMG mapping of muscle denervation. As the lesion involves the L_6 spinal nerve and the lumbosacral trunk (which together contribute to the origin of the gluteal and obturator nerves), denervation will occur in muscles supplied by both nerves (obturator nerve - adductor, pectineus, and gracilis muscles; gluteal nerves - gluteal muscle group). These features serve to distinguish a lesion at this level from a lesion affecting the main trunk of the sciatic nerve (see Figure 11.6 and **F** below).

Many animals suffer severe pelvic fractures, including bilateral sacroiliac luxations or ilial shaft fractures, but never show neurological deficits. It is obviously futile to predict that a neurological deficit will occur in any given case with a pelvic fracture. However, the presence of the above fracture types should give the clinician a high index of suspicion, and certainly indicate the need for a thorough neurological examination. If a sciatic-type deficit is diagnosed, it is highly likely to be related to the fracture or luxation. A severe neurological deficit considerably complicates the management of a dog with pelvic fractures, particularly if there are associated long bone fractures of either pelvic limb. Early recognition of neurological complications allows proper client communication and education. In particular, the increased recovery period and additional nursing care must be discussed.

General orthopaedic recommendations as to whether to perform internal fixation of the pelvic fracture or luxation should be followed. Surgery may allow visualisation of the injured intra-pelvic nerves, but simple anastomosis is not feasible in crush or traction injuries. Recognition of a severed nerve trunk can justify limb amputation.

Stabilisation of pelvic fractures might be expected to reduce repeated trauma to the already-damaged nerve trunks. This is not necessarily supported by the results of one survey. The results were good or excellent in 11 of 13 dogs that underwent surgery, recovery occurring after 2-16 weeks of rehabilitation. However, 10 of 12 dogs that did not have surgery had similar results over 2-12 week periods. This suggests that the bulk of the nerve damage occurs at the time of the original injury and that it does not seem to be exacerbated by an unstable fracture. Overall, 81% of 34 dogs and cats had excellent or good recovery of neurological deficits following pelvic fractures (Jacobsen and Schrader 1987).

In another series, 7 of 11 patients with sciatic paralysis associated with ilial shaft fracture recovered within six months and an eighth within 12 months. Three of four cases with sacral wing fractures or sacroiliac luxation also recovered within six months. Some animals with a predominantly peroneal distribution to their weakness learn to compensate by flipping the paw, to prevent knuckling of the digits (Sharp 1982; Gilmore 1984).

It is possible to cause iatrogenic damage to this area of the plexus during repair of pelvic or sacral fractures. In addition, the callus associated with a healing ilial shaft fracture can compress nerves at this site. These are two further reasons why preoperative identification of potential neurological deficits is very important.

F: Injury to the main trunk of the sciatic nerve

The sciatic nerve is vulnerable to injury after it leaves the pelvis, although injury here occurs less frequently than does injury to the more proximal structures discussed under **E** above. A large number of causes of sciatic nerve damage have been documented as shown in Table 11.4.

Table 11.4: Causes of injury to the sciatic nerve.

Intramedullary pinning of the femur
Ischial fractures
Acetabular fractures
Craniodorsal hip luxation
Surgery of the hip area
Triple pelvic osteotomy
Perineal hernia surgery
Bites and lacerations
Femoral neck fracture
Femoral shaft fracture
Intramuscular injection
Rabies vaccination

The most important are either complications resulting from intramedullary pinning (Fanton *et al* 1983), or from ischial and acetabular fractures (Chambers and Hardie, 1986). Clinically, these injuries may be indis-

tinguishable from those occurring to the intra-pelvic portions of the sciatic nerve covered under area **E**.

Conscious proprioceptive deficits, selective muscle atrophy, reduced hock flexion, and possibly reduced sensation over the sciatic or peroneal field are seen. Radiography is useful to identify any recent or old orthopaedic injuries. Sacral deficits do not occur in association with pure sciatic nerve lesions, unless another injury is also present. The main means of differentiating a sciatic nerve lesion from a more proximal lesion (such as **E** above) is that in sciatic nerve injury there is no dramatic neurogenic muscle atrophy, and no EMG evidence of denervation in muscles supplied by the gluteal nerves (gluteal muscle group), obturator nerve (adductor group) and sacral nerves (sacrococcygeus muscle group).

Intramedullary pinning and sciatic neuropathy - a 14.5% incidence of sciatic neuropathy was reported in one series of 83 femoral fracture repairs. All pins had been placed in a retrograde fashion. The onset of signs was immediate in three animals and delayed for 1-50 days (mean 16 days) in eleven. All cases showed pain over the greater trochanter area and all showed deficits referable to the sciatic field alone. Surgical exploration confirmed trauma from pin insertion as the cause in three cases and from cicatrix formation around the exposed pin in eleven. All animals improved following external neurolysis and pin removal or shortening, and no animals were left with permanent neurological deficits (Fanton *et al* 1983). Although excessive pin length was thought likely to be a contributory cause of the nerve damage, this was not proven. Sciatic nerve damage from this cause can be minimised by keeping the femur in adduction and the hip in a ventral position during pin placement. External rotation of the hip during pin replacement should be avoided. Retrograde pinning has been shown to be more likely to cause sciatic damage than normograde pinning (Palmer *et al* 1988).

Acetabular or ischial fractures - these are occasionally associated with sciatic neuropathies. In a series of seven cases of sciatic neuropathy due to ischial or acetabular fractures, four of the cases were caused by the fracture itself and in the other three the sciatic nerve became entrapped by progressive fibrosis at the fracture site. Cranial displacement of the ischiatic tuberosity caused compression at the greater trochanter in five of the dogs. Diagnosis in each case was confirmed by an EMG pattern of denervation typical for damage to the main trunk of the sciatic nerve at this level, with sparing of the gluteal muscles. In some cases, denervation was also absent in the hamstring muscle group, presumably because the branch to these muscles had left the sciatic nerve above the site of compression (Figure 11.6). Surgical exploration was performed on a delayed basis in each case and all lesions were demonstrated between the sacrotuberous ligament and the third trochanter. Limb amputation was performed in one dog and external neurolysis in the other six. The superficial gluteal muscle was used to protect the nerve in two dogs and a nerve cuff was utilised in one. All dogs had satisfactory return to function (Chambers and Hardie 1986).

Intramuscular injections in the caudal thigh carry a significant risk of damaging the sciatic nerve. For this reason, other injection sites are preferable. Intrafascicular injection can result in severe nerve damage with permanent disability, particularly with certain preparations, for example, penicillin / streptomycin and anthelmintics. Other drugs, for example, soluble corticosteroids, seem to be less irritant.

Perineal hernia repair - the sciatic nerve lies very close to the sacrotuberous ligament and can easily be damaged by attempts to pass a suture around this ligament. If this structure must be used in hernia repair, then the suture should be carefully passed through the ligament, and not around it.

Triple pelvic osteotomy has been reported as a cause of delayed sciatic neuropathy in one dog. External neurolysis was successful in reversing the neurological deficit (Cockshutt *et al* 1993).

Following rabies vaccination - an important, though fortunately very uncommon LMN disorder can follow rabies vaccination using live virus derived from chick embryo (Erlewein 1981). Clinical signs appear 7-21 days post vaccination and begin in the pelvic limb following vaccination in the ipsilateral thigh. LMN signs are seen initially as the virus travels in the peripheral nerves to reach the spinal cord, and generalisation can occur later. At present there is no evidence to suggest that the virus reverts to field virulence, and recovery has been documented in dogs within one or two months. Appropriate notification of public health authorities should be made. Natural infection could mimic the early features of this syndrome.

Distal lesions - injuries to the tibial division of the sciatic nerve are rare. Bilateral tibial nerve deficits are commonly seen in feline diabetic neuropathy. The clinical features are described above. The peroneal nerve is more vulnerable than the tibial division due to its more superficial location at the head of the fibula. Pressure from an orthopaedic cast, surgery of the stifle joint particularly cruciate repair, or an injury in this area, can all result in the clinical features described. However, the majority of cases with peroneal-type deficits have, in reality, sustained injury to the main trunk of the sciatic nerve or its origins.

Surgery for Lesions of the Lumbosacral Plexus

Exploration of the sciatic nerve

This nerve is easily located under the biceps femoris muscle during a standard approach to the proximal and mid-shaft portions of the femur. More proximal exposure is obtained by extending this into a caudolateral approach to the hip joint, where the incision through the fascia lata is continued caudal to the greater trochanter. The origin of the biceps femoris muscle on the sacrotuberous ligament is freed, taking care at this point to protect the caudal gluteal vessels. A tenotomy of the superficial gluteal muscle allows maximum exposure of the sciatic nerve. If more exposure is required at this point, a middle gluteal tenotomy can be performed. However, the more muscle mass that is cut, the more adhesions that will form at this level, which may subsequently risk entrapment of the nerve.

Exposure of the lumbosacral trunk area is difficult but can be obtained by a ventrolateral approach to the ilial shaft, if necessary combined with an ilial osteotomy.

Following exposure of the nerve, any fibrous scar or callus should be carefully dissected free. To protect the sciatic nerve from subsequent adhesions, the superficial gluteal muscle can be passed under the nerve to keep it in a more superficial position (Chambers and Hardie 1986). A silicone nerve cuff can also be used to protect the nerve. It should be laid around the damaged area and not be too tight. A cross sectional area of two to three times that of the nerve itself is recommended. Therefore for a nerve of 6mm diameter, a cuff of between 8 and 10 mm diameter is ideal. The cuff should be anchored with fine epineural sutures of (8/0) polypropylene or nylon.

Muscle relocation

Two techniques have been described to overcome peroneal nerve paralysis. The first attaches the tendon of the long digital flexor muscle, which is innervated by the tibial division of the sciatic nerve, to that of the long digital extensor muscle (Bennett and Vaughan 1976). This technique may be of value if the tibial division of the sciatic nerve is functional, as determined by minimal muscle atrophy and normal nerve conduction studies. The major problem with this technique is that many animals with severe peroneal nerve dysfunction usually have a sciatic neuropathy, and have also sustained some degree of clinical or subclinical tibial nerve dysfunction. This usually prevents the long digital flexor from functioning adequately in its new role.

Complications associated with injuries to the lumbosacral plexus are similar to those encountered in the thoracic limb or described above.

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CHAPTER TWELVE

Visceral and Bladder Dysfunction Dysautonomia

Nicholas J. H. Sharp and Jody L. Gookin

VISCERAL AND BLADDER DYSFUNCTION

This section discusses neurogenic abnormalities affecting the bladder, colon and rectum. More detailed reviews exist, particularly of the physiology and the effect of neural damage on micturition. It is not the aim of this chapter to duplicate these reviews, but to provide a simplified overview. This would seem justified because several aspects of the physiological control of micturition still remain controversial and poorly understood.

Anatomy

The anatomy of the lumbosacral plexus has been described in Chapter 11.

Motor innervation

The pelvic viscera have three main sources of motor innervation (Figure 12.1):

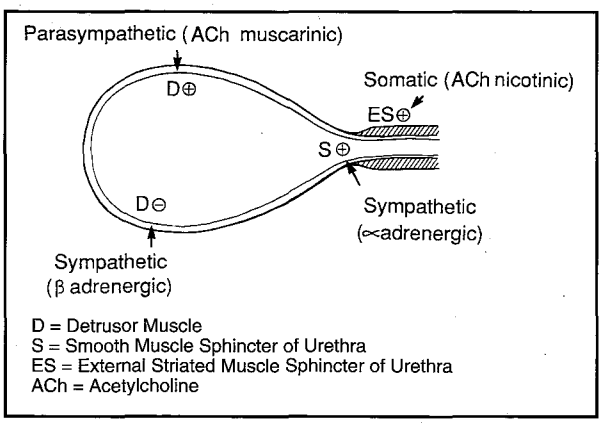

Figure 12.1: Diagram to show the innervation of the bladder and proximal urethra

- **Pelvic nerves** arise from the sacral spinal cord segments S_1-S_3 and supply parasympathetic innervation to the bladder, rectum and genital smooth muscle
- **Hypogastric nerves** arise from lumbar segments L_1-$L_{4/5}$ and supply sympathetic innervation to the bladder, rectum and genital smooth muscle.
- **Pudendal nerves** arise from segments S_1-S_3 and supply somatic innervation to external anal and urogenital skeletal muscle.

The three most important target organs in the lower urinary tract for motor innervation are:

- **Detrusor smooth muscle** of the bladder, which is made to:
  relax by sympathetic stimulation (beta effect)
  or contract by parasympathetic stimulation
- **Urethral smooth muscle** is made to contract by sympathetic stimulation (alpha effect)
- **Urethral striated muscle** that contracts via pudendal nerve stimulation.

Autonomic stimulation of smooth muscle, for example the detrusor muscle, occurs by diffusion of transmitter from terminal nerves to adjacent muscle cells. This induces a wave of depolarisation within the detrusor muscle, the spread of which is facilitated across "tight junctions" between the cells. If the bladder wall is over-stretched, these tight junctions are damaged and the detrusor muscle becomes unresponsive. If the stretch is not reversed within 1-2 weeks, fibrosis may occur, which will permanently disturb detrusor function.

Sensory innervation

These nerves also carry sensory nerve fibres, which enter the spinal cord at either the sacral or lumbar levels.

Physiology of Micturition

The course of events leading to micturition are as follows:

- As the bladder passively fills with urine, there is initially only a gradual increase in intravesicular pressure. This is largely because the detrusor muscle relaxes, due to beta adrenergic (sympathetic) activity (Figure 12.1).
- As the bladder nears maximum capacity, tension in the detrusor muscle increases more rapidly until a threshold level is reached. Sensory fibres in the bladder wall respond to this increase in tension, and at threshold level they

activate parasympathetic neurons in the sacral spinal cord. This information is then relayed to the brain stem (pons).

- Reflex efferent stimulation from the brain stem to the sacral cord facilitates firing of parasympathetic neurons and results in sustained detrusor muscle contraction.
- Sensory stimulation of bladder wall stretch receptors also reflexly inhibits both sympathetic and pudendal nerves, resulting in sphincter relaxation.
- Higher control via the brain stem is important to sustain detrusor contraction and to co-ordinate it with sphincter relaxation. The bladder therefore empties against a low sphincter pressure.
- When the bladder is empty, its sensory nerves stop discharging and urethral receptors also perceive that urine flow has stopped.
- Parasympathetic stimulation then stops, and the activity of sympathetic and pudendal nerves increases. Thus the bladder relaxes to allow refilling to occur, and the sphincter closes.
- The cerebral cortex can initiate the micturition reflex as it does during territorial marking, or it can inhibit micturition as in house training.

Micturition Disturbance due to Spinal Cord Lesions

"Micturition fibres" running in the spinal cord are usually more resistant to the effects of injury than proprioceptive or motor fibres. Therefore, most dogs develop ataxia, paresis and paraplegia before they lose full control of urination. Some fine tuning of the micturition reflexes may be lost at an earlier stage.

Full control of urinary continence is lost before the loss of pain sensation caudal to a spinal cord lesion, as micturition fibres are damaged before those carrying deep pain sensation. The prognosis for recovery from spinal cord lesions deteriorates as the paraplegic animal first loses control of continence, then deep pain sensation.

Examination of the Neurogenic Incontinent Patient

Before assessing if the animal has neurological disease, consider that there could be a non-neurogenic cause for the abnormal micturition, for example infection, obstruction or ureteral ectopia (Holt 1992). The patient evaluation should be approached in three stages - clinical history, clinical examination and ancillary diagnostic aids.

Clinical history

This information is particularly important to obtain in a recumbent or paraplegic animal, or one with sacral or pelvic fractures. Careful questioning of the owner and observation of the animal can provide much of the information necessary to determine the level of neurological damage.

Cerebral function - discover whether the animal shows any cerebral recognition of the need to urinate, such as showing discomfort, vocalising or attempting to get outside before urinating. Such a demonstration of house training may be displayed by a continent recumbent or paraplegic animal, which will remain dry until it is eventually forced to urinate on itself or its bedding. Conversley, some owners will state that an animal is continent, because every time they pick it up, it urinates. The chances are that if this voiding occurs immediately (and often over them), then it is simply the increase in abdominal pressure or the tactile stimulation of lifting that has caused voiding, and that the animal is in fact incontinent. If, however, the animal attempts to wait until it is outside, this may be a sign of partial or returning cerebral control.

Detrusor function - if the animal does void urine, does it pass a good volume in a steady flow? In other words, is the detrusor functioning properly? This is distinct from continuous leakage of urine, an important feature that relates to either overflow of urine due to an UMN lesion (see below) or sphincter incompetence.

Sphincter function - is the animal capable of stopping urination if distracted or made to walk while voiding? If so, integrity of the external urethral sphincter pathways has been demonstrated. Leakage of urine implies insufficient sphincter tone (striated or smooth muscle or both). This assessment should not be made when the bladder is grossly distended or there is high intravesicular pressure.

All of this information can be obtained without touching the animal and is a very important facet of assessment of any neurological case. The ability to void and the degree of overflow have, therefore, already yielded information regarding the animal's degree of cerebral control, detrusor function, and sphincter integrity.

Clinical Examination

By careful physical examination, one can now determine:

- If the animal appears to urinate voluntarily, palpation of the bladder at the end of urination will identify the presence of any residual urine. The latter can be quantified by catheterisation and should be less than 0.2-0.4 ml/kg in dogs and less than 2 mls total in cats. Ultrasonography, if available, gives a very rapid and noninvasive estimate of residual bladder volume.
- Manual expression of the bladder on a separate occasion gives subjective information on whether sphincter tone is normal, increased or decreased.
- A careful neurological examination will define

whether a UMN or a LMN lesion is present. Incontinence is highly likely if the anal reflex and perineal sensation are absent.

Ancillary diagnostic aids

These include clinical pathology tests such as a complete blood count, serum BUN and creatinine, urinalysis and culture. These may identify systemic illness, sepsis or renal disease. Survey and contrast radiography and ultrasonography may also be of value to identify associated orthopaedic injuries or genitourinary tract abnormalities.

The dynamics of the micturition reflex can be quantified using more sophisticated techniques, explained in Chapter 4. However, much of this information (i.e. presence of a detrusor reflex, sphincter tone) can be qualitatively obtained from the history and physical examination.

Types of Micturition Abnormality

For simplicity, the terms UMN and LMN will be employed. The micturition abnormality can be classified according to whether the detrusor or sphincter function is depressed, normal or increased (Table 12.1)

I. UMN Lesion - Cerebral cortex

- Detrusor - normal
- Sphincter - normal

Aetiology - brain lesions.

Signs - loss of house training, due to lack of cortical control of the micturition reflex. These animals tend to urinate with equal frequency throughout the day and night.

II. UMN Lesion - Thoracic or lumbar spinal cord

- Detrusor - absent (initially)
- Sphincter - normal or hyperactive

Aetiology - e. g. disc herniation, fracture or vascular lesion interfering with micturition fibres.

Following severe thoracic or lumbar spinal cord damage in animals, a phenomenon called "spinal shock" temporarily abolishes the detrusor reflex. The anal, pedal and patellar reflexes are not affected by this phenomenon, whereas in humans all spinal reflexes are lost.

Signs - initially the bladder fills until intravesicular pressure exceeds sphincter pressure and causes urine to overflow (often termed urinary retention with overflow - UR+O). This is because no detrusor reflex is activated. Raising the intra-abdominal pressure (e.g. when the animal is picked up) will also often cause an overflow of urine. The animal is incontinent and unaware of bladder filling.

Prognosis - if the spinal cord lesion is reversible, recovery of continence can occur. If the lesion is irreversible, a reflex or "automatic" bladder may result. This usually occurs within three or four weeks of the original spinal cord injury as the detrusor reflex at the spinal level recovers and starts to function, but now without higher control. With a reflex bladder:

- Emptying occurs without the animal's knowledge.
- Sustained detrusor function and complete emptying may not occur, so residual volume is high.
- Lack of higher control on the pudendal reflexes may cause hypertonicity of the external sphincter (just as may occur to the patellar reflex in a UMN lesion), which further counteracts proper emptying. Failure of sphincter relaxation may cause high intravesicular pressures to develop, favouring a reflux of urine up one or both ureters with the risk of pyelonephritis.
- High sphincter tone, if present, may make manual evacuation difficult or even dangerous.

Table 12.1: Classification of micturition abnormality.

LESION LOCATION	DETRUSOR FUNCTION	SPHINCTER FUNCTION	RESIDUAL URINE	ANAL REFLEX
I UMN - cerebral	Normal	Normal	Normal	Normal
II UMN -TL spinal cord	-	Normal or ++	++	Normal
III LMN - cauda equina	-	-	++	-
IV LMN sphincter	Normal	-	Normal	Variable
V LMN detrusor	-	Normal	++	Normal

Key - = absent or none
++ = increased

Treatment - it is crucial to keep bladder volumes low at all times by frequent manual expression. Skeletal muscle relaxants or adrenergic blockers are usually employed to facilitate this, by lowering sphincter tone. Urinary tract infection is almost certain to occur and should be identified by regular urinalysis and culture. Use of antibiotics as prophylaxis is contraindicated as it will only select for resistant organisms.

Note - in acute and chronic UMN lesions, the anal reflex is intact and urethral sphincter tone will be perceived as normal or increased on manual expression. These features should differentiate it from a LMN lesion.

In dogs with only mild to moderate paresis, the stream of urine may spurt or stop abruptly. This is due to poor co-ordination of detrusor contraction and sphincter relaxation and has been loosely termed reflex dyssynergia.

III. LMN Lesion - Sacral cord or cauda equina

- Detrusor - absent
- Sphincter - absent

Aetiology - e.g. sacral fracture, sacrocaudal fracture / luxation or ischaemic injury damaging the sacral spinal cord segments or nerve roots.

Clinical signs - typically the detrusor and anal reflexes are absent. The bladder will fill and overflow easily due to the low external sphincter tone, and manual expression meets little resistance at all bladder volumes. This is in contrast to the Type II UMN lesion, where manual expression is difficult unless intravesicular volume (and pressure) is high.

Less severely damaged animals will retain some external urethral (and anal) sphincter tone, as assessed by resistance to manual expression, and generally have a more favourable prognosis than animals lacking sphincter tone. For more information regarding prognosis see Chapter 11. Occasionally, animals with injuries at this level show a paradoxical increase in sphincter tone for reasons that are not clear.

Treatment - the most important principle is again to keep the bladder volume low at all times by regular manual expression. Bethanechol may be of value to stimulate detrusor function. Skeletal muscle relaxants like dantrolene or diazepam, or less commonly alpha adrenergic blockers, may be helpful in cases with a paradoxical increase in sphincter tone.

IV. LMN Lesion - Failure of urethral sphincter

- Detrusor - present
- Sphincter - absent

Aetiology - e.g. hormonally responsive incontinence, seen mainly in neutered animals.

Clinical signs - the sphincter is usually only intermittently incompetent, and subject to leakage only under emotional stress or high abdominal or intravesicular pressures. The animal is otherwise continent and the residual volume is normal. Manual expression is relatively easy. Occasionally the anal reflex is depressed or absent.

Treatment - oestrogen or testosterone therapy may be employed, or an adrenergic drug may be of value. Colposuspension should also be considered.

Note - FeLV-associated urinary incontinence in cats falls into this category. It is usually unresponsive to hormone supplementation (see below).

V. LMN Lesion - Failure of detrusor function

- Detrusor - absent
- Sphincter - normal

Table 12.2: Drugs used to treat micturition abnormalities.

DRUG	ACTION	DOSE
Dantrolene	Relax - external (skeletal muscle) sphincter	Dog - 1-5 mg TID Cat - 0.5 to 2 mg/kg TID
Diazepam	Relax - external (skeletal muscle) sphincter	2-10 mg TID
Phenoxybenzamine	Relax- internal (smooth muscle) sphincter	0.5 mg/kg TID
Phenylpropanolamine	Stimulate - internal (smooth muscle) sphincter	12.5 - 50 mg TID
Diethylstilboestrol	Stimulate - internal (smooth muscle) sphincter	0.1-1.0 mg for 3-5 days, then 1mg per week
Oestradiol cypionate	Stimulate - internal (smooth muscle) sphincter	0.1-1.0 mg
Testosterone	Stimulate - internal (smooth muscle) sphincter	2.2 mg/kg
Bethanechol	Stimulate - detrusor muscle	2.5-10 mg TID S/Q or 2-15 mg TID PO

Aetiology - either idiopathic detrusor failure or secondary to functional urethral obstruction. The end result is bladder over-distension, which may then damage the tight junctions of the detrusor muscle.

Clinical signs - inability to empty the bladder and onset of an overflow incontinence. The animal is aware of bladder filling as sensory function remains, and so makes repeated unsuccessful attempts to void. The anal reflex is intact.

Treatment - an indwelling urethral or cystostomy catheter for several days, together with bethanechol and phenoxybenzamine, are the suggested therapy.

Specific Conditions Associated with Urinary Incontinence

Urinary incontinence in FeLV-positive cats

This has been described together with anisocoria and atonic pupils (Barsanti and Downey 1984). The incontinence is intermittent in nature, usually consisting of dribbling while recumbent, asleep or when excited. Urination is otherwise normal. Although this appears similar to hormonally-responsive incontinence, half of the female cats in the series were entire and the neutered males did not respond to testosterone. Also, a hormonal aetiology does not account for the anisocoria. The lesion seems to be at the level of the pelvic ganglia.

Feline and canine dysautonomia

This is covered more fully later in this chapter. The incidence of dysuria in dysautonomia varies from 17-39% in cats and is higher in dogs. Affected cats are usually FeLV negative. The urinary dysfunction is due to lack of motor innervation to the bladder and urethra from the parasympathetic, sympathetic and in some cases also the somatic (pudendal) centres. This resembles the incontinence seen in category III above (such as with a sacral fracture), except that the sensory nerves are much less severely affected in dysautonomia. Therefore, most incontinent cats with dysautonomia are aware of bladder filling and make repeated attempts to void by abdominal muscle contraction. Due to an absent detrusor reflex, the residual volume is high and lack of sphincter function renders manual expression easy in most cases. Combinations of bethanechol and phenoxybenzamine may aid affected animals, but the most useful treatment is frequent, careful manual expression of the bladder combined with nursing care to prevent urine scalding.

Management of Neurological Incontinence

Over distension of the bladder can cause permanent damage by disrupting the tight junctions of the detrusor muscle and later by inducing fibrosis. It is imperative that this is never allowed to occur. Incontinent animals with elevated residual volumes are also prone to severe and even potentially life-threatening urinary tract infections. The aim should be to empty the bladder completely at least three and preferably four times daily. With manual evacuation, it is useful occasionally to check the efficiency of expression by catheterisation of the patient at the end of the procedure. Manual expression may be difficult or dangerous when sphincter pressure is high. In animals with raised sphincter pressure that have not responded to pharmacological blockade, catheterisation is indicated.

Intermittent aseptic catheterisation is the method of choice in those instances where manual expression is either impossible or undesirable. An indwelling catheter may be easier in females but should only be used for one or two days and must be connected to a closed urine collection system. An indwelling catheter is very likely to introduce infection if maintained for more than two days. Use of antibiotics in such patients would only select for a resistant strain of bacteria and would not eliminate the infection.

The possibility of infection should be monitored by regular urinalysis combined with urine culture when inflammatory changes are detected. Antibiotic therapy should be guided by sensitivity testing, with amoxycillin or trimethoprim-sulpha being good initial choices. Therapy should be maintained for an adequate duration (14 days) to eliminate the infection completely, and a repeat culture should be performed seven days after the end of therapy. Antibiotic prophylaxis is not warranted and under no circumstances should it replace proper nursing care. Rigid attention to nursing in order to prevent urine scalding by the use of proper bedding materials, regular bathing, drying and application of emollients and / or petroleum jelly, should be performed three or four times daily (Wheeler and Sharp 1994).

Pharmacological Manipulation of Micturition Reflexes

As can be seen in Figure 12.1. the main neural control of the urinary tract is mediated by:

- Beta adrenergic sympathetic relaxation of the detrusor muscle
- Acetylcholine-induced (muscarinic) parasympathetic stimulation of the detrusor muscle
- Alpha adrenergic sympathetic stimulation of the smooth muscle internal urethral sphincter
- Acetylcholine-induced (nicotinic) somatic stimulation of the striated muscle external urethral sphincter.

Drug Treatment of Neurogenic Incontinence

Skeletal muscle relaxant - dantrolene

This relaxes the striated muscle external urethral sphincter and so helps to reduce overall sphincter

tone. This drug can cause hepatic enzyme elevation in humans. Other drugs that may have value are diazepam, methocarbamol or acepromazine. Overdose of these may result in weakness or tranquillisation.

Alpha blocking agent - phenoxybenzamine
This will block the alpha adrenergic sympathetic stimulation of urethral smooth muscle, and therefore help reduce sphincter tone. Potential side effects include hypotension.

Alpha stimulation - phenylpropanolamine
This drug acts by stimulating alpha adrenergic receptors to increase tone in the urethral smooth muscle. Potential side effects are urinary retention, anorexia and systemic sympathetic stimulation.

Hormonal therapy

Diethylstilboestrol - oestrogens act by facilitating alpha adrenergic receptor function, and so increase smooth muscle sphincter tone. This may be valuable in some bitches, although side effects of oestrus or bone marrow suppression should be monitored. Beneficial effects may be transient.

Oestrodiol cypionate - is a more powerful oestrogen than diethylstilboestrol with a higher potential risk of oestrogenic side effects.

Testosterone - as depotestosterone cypionate used parenterally at intervals of weeks or months depending on response. It should be used with care where perianal adenomas or prostatic disease are present.

Parasympathetic stimulation - bethanechol
This is the most effective drug to selectively stimulate the detrusor muscle. General stimulation of the parasympathetic nervous system can occur with overdose. This can be countered with atropine. Bethanechol often exaggerates dyssynergia and therefore is routinely combined with phenoxybenzamine.

Neural Disturbances of Defecation

The colon and rectum are innervated by the sympathetic and parasympathetic nervous system in a similar manner to the bladder. However, the intrinsic neurons in the myenteric plexus of the gastrointestinal tract also play an important role in maintaining motility. The colon and rectum therefore appear to be less dependent on higher control in order to empty themselves. Even long term denervation at either the sacral level or higher usually causes surprisingly few problems. Presumably, this is due to the fact that periodic incomplete emptying and elevated residual volume are much less of a problem than they are in the denervated bladder.

Megacolon
This is defined as an enlarged colon where there is abnormal retention of contents. It is divided into two categories, congenital and acquired.

Congenital megacolon has not been documented to date in dogs or cats. It is described in humans, horses and mice. It results when a portion of foetal colon is not innervated by ganglion cells during their migration from the neural crests (Hirshchsprung's disease). The affected colon remains permanently contracted, causing obstruction to the normal passage of faeces and dilation of the proximal portions of colon.

Acquired megacolon occurs most often in cats where an obstruction causes prolonged distension of the colon or rectum. The obstruction could be an inflammatory or neoplastic stricture, pelvic canal narrowing following a pelvic fracture, or idiopathic in nature (Holt and Johnson 1991).

Feline dysautonomia
Constipation is a common feature in this disorder and presumably relates to the general reduction in autonomic tone, loss of intrinsic gut neurones and dehydration.

Damage to the spinal cord or cauda equina
Animals with lesions at the thoracic or lumbar area usually develop reflexive emptying, often in response to tactile stimulation of the pelvic or perineal area. Most of these animals can be managed by diet alone.

Treatment
Although the colon and the rectum appear able to empty spontaneously after denervation, it is important to prevent constipation. Ensure adequate fluid balance, and feed moist food together with a stool softener such as Isogel® or bran, to give a bulky yet soft stool. Liquid paraffin may aid lubrication of dry faeces while enemas may relieve any periodic blockage. If the blockage is severe, gentle manual evacuation under general anaesthesia may be required and in exceptional cases, a colotomy may prove necessary. In acquired megacolon, removal of the obstruction, e.g. correction of prostatomegaly or reduction of a pelvic fracture, should improve the situation. Cats with idiopathic megacolon often respond well to subtotal colectomy.

DYSAUTONOMIA

Several localised dysautonomias are well recognised in small animals, including Horner's syndrome, and FeLV - associated tonic pupils. Localised sympathetic disturbance is also seen following brachial plexus root avulsion, or with severe unilateral cervical spinal cord injuries where vasomotor tone to affected limbs is lost. This can result in profound vasodilation and up to a 10°C increase in limb temperature. After several weeks

the limb is likely to become subnormal in temperature, as vascular pooling becomes the predominant effect.

Feline Dysautonomia

Key and Gaskell in 1982 were the first to draw attention to this disorder. Now known as feline dysautonomia, the condition appears to be less common than it was in the 1980's, and there is evidence to suggest that its clinical severity has also lessened (Baxter and Gruffydd Jones 1987). The pathophysiology and underlying pathological changes appear almost identical to canine dysautonomia, grass sickness of horses, and the newly recognised dysautonomia in hares. Feline dysautonomia has been recognised throughout Europe, although the vast majority of confirmed cases have been reported from the United Kingdom. Isolated cases have also been documented from the United States of America, the United Arab Emirates, and New Zealand. There is no sex or breed distribution. Animals less than three years of age appear to be more susceptible but a wide age range from 6 weeks to 11 years has been recorded (Waltham Symposium 1987).

Epidemiology

Direct contagion is not supported by epidemiological studies, and no common environmental or management factor has been identified.

Aetiopathogenesis

This remains unknown although a toxic or viral agent cannot be ruled out (Pollin and Griffiths 1992). Whatever the causal factor, it appears to have a primary effect on the pathways for protein biosynthesis in affected neurones. There is no evidence that a particular neurotransmitter is selectively inhibited and, furthermore, pharmacological studies have demonstrated that the receptors in tissues denervated by this condition are still functional (Waltham Symposium 1987).

The autonomic nervous system provides motor innervation to visceral smooth muscle, cardiac muscle and glands (Figure 12.2). Clinical signs reflect dysfunction of both the sympathetic (e.g. third eyelid prolapse, bradycardia) and parasympathetic (lack of ocular, nasal and oral secretions) divisions of the autonomic nervous system. Non-autonomic deficits referable to the somatic nervous system are also seen to a lesser extent (e.g. anal areflexia, pelvic limb proprioceptive deficits).

Clinical features

The onset of signs varies in rapidity from a few hours to several weeks. Some cats show prodromal mild upper respiratory or gastrointestinal signs, due to either irritation or autonomic hyperactivity. This is usually manifest as serous oculonasal discharge or diarrhoea. Dilated pupils, oesophageal dysfunction, dry nose, reduced lacrimal secretions, prolapse of the third eyelid, regurgitation and constipation were seen in over 75% of the cases documented prior to 1984 (Rochlitz 1984; Sharp *et al* 1984). The clinical severity

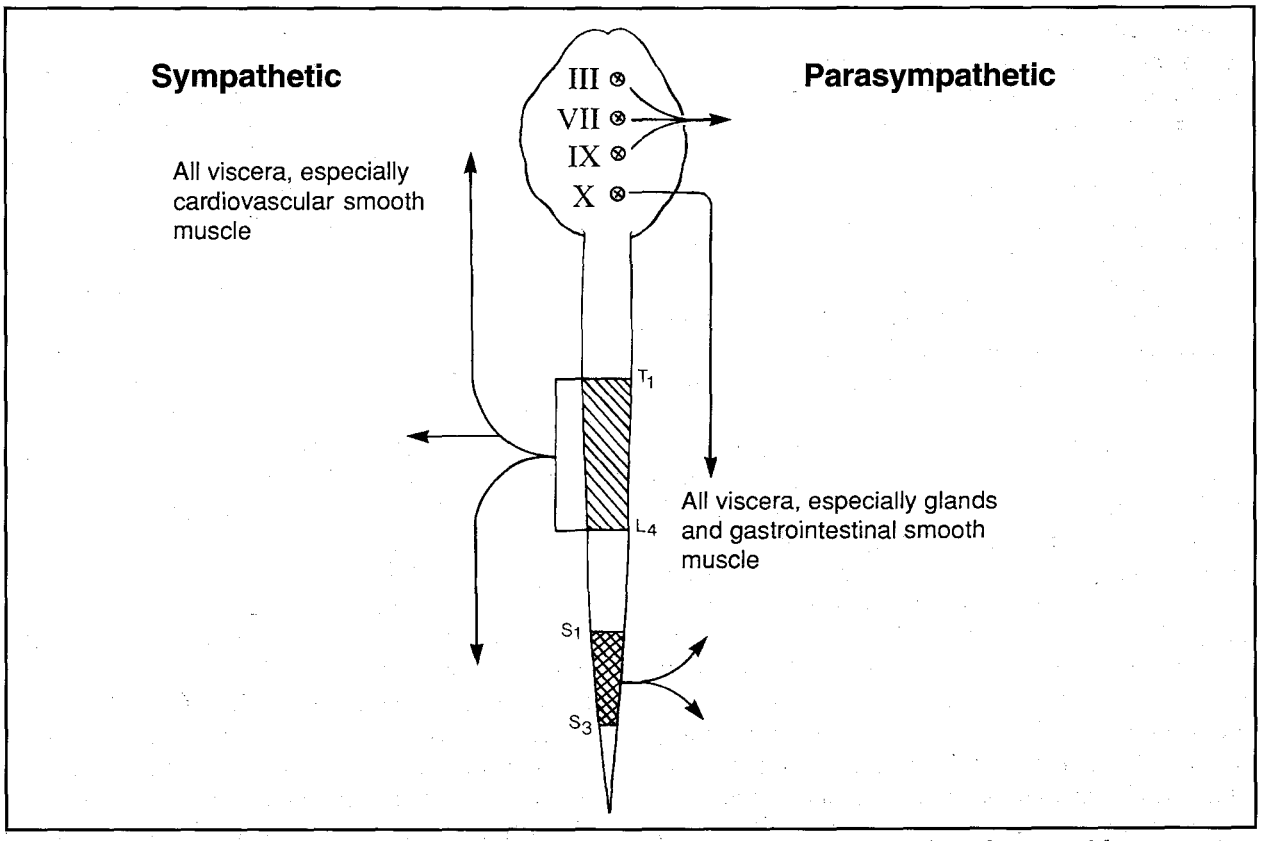

Figure 12.2: Diagram to show the origins and distributions of the sympathetic and parasympathetic divisions of the autonomic nervous system.

seems to have lessened more recently, with each of these features being seen in less than 60% of more recently affected cats. The one clinical feature that appears to have increased in frequency is dysuria (Baxter and Grufydd Jones 1987).

Diagnosis

Initially, diagnosis was based on the unusual combination of clinical features seen in this condition. However, in less severely affected cats, such as those encountered more recently, an objective means of diagnosis may be required. A scoring system for the various clinical signs that are commonly associated with feline dysautonomia has been developed (Table 12.3). The clinical features have been divided into two groups. Group A consists of features that are either objective or frequently encountered in feline dysautonomia, but are otherwise uncommon in the cat. Features in group B are less frequently encountered in the condition or more likely to be associated with other disorders. In combination, however, the features in group B would be very suggestive of feline dysautonomia. Using this system, the criteria necessary for a positive clinical diagnosis of feline dysautonomia are a total score of nine or more (grades 3 or 4). In the absence of another lesion to explain the clinical signs, such as a compressive lesion of the cauda equina, grade 2 suggests a probable diagnosis of dysautonomia. A score of between one and four gives an inconclusive clinical diagnosis. This system allows the severity of the disease in individual cases to be characterised according to their overall grade from 1 (mild) to 4 (severe). Definitive diagnosis for feline dysautonomia at present requires histopathological confirmation of the pathognomonic lesions in autonomic ganglia.

In equivocal cases, the most objective criteria are contrast radiography of the oesophagus and the presence of reduced lacrimal secretions. The latter is assessed using the Schirmer tear test - see Chapter 9. Oesophageal dilation affects primarily the intrathoracic portion of the oesophagus, as demonstrated by survey radiography and by contrast studies. In some cats dysfunction is mild and restricted to retention of a small pool or bolus of contrast agent beyond five minutes. In other animals, contrast may be retained for over 24 hours and dysfunction of the cervical oesophagus may also be seen. Aspiration pneumonia may be detected on thoracic radiography. A number of cats show evidence of delayed gastric emptying on barium contrast study. Small intestinal transit time is variable. Distension of the urinary bladder, colon and rectum may also be demonstrated on abdominal radiography.

Further evaluation by pharmacological testing may be useful in certain instances. Atropine often results in an absence of reflex tachycardia if the heart lacks sympathetic tone, but has the disadvantage of exacerbating parasympathetic dysfunction. The phenomenon of denervation hypersensitivity can also aid diagnosis (Canton and Sharp 1988; Guilford *et al* 1988). Any target organ will become supersensitive to its physiological transmitter substance if it is deprived of that transmitter due to partial or complete denervation.

Table 12.3 Grading System for feline dysautonomia

Group A Clinical Features	
	Score
1. Dry, crusty nose	2
2. Reduced tear secretion (<5mm/min) on Schirmer tear strip	2
3. Mydriasis or reduced pupillary light response	2
4. Bradycardia <120 beats/min	2
5. Regurgitation with oesophageal dysfunction on contrast radiography	2
Group B Clinical Features	
6. Constipation	1
7. Proprioceptive deficits	1
8. Dry oral mucosae	1
9. Prolapsed membrana nictitans	1
10. Dysuria or bladder atony	1
11. Anal arreflexia	1
Maximum possible	16

Score	**Clinical Grade**	**Clinical Diagnosis**
1 - 4	1	Inconclusive
5 - 8	2	Probable
9 - 12	3	Positive
13 - 16	4	Positive

Two ocular pharmacological tests based on the presence of denervation hypersensitivity are useful:

- ciliary smooth muscle frequently becomes supersensitive to acetylcholine due to the parasympathetic denervation. A 0.1% solution of pilocarpine, which mimics the muscarinic action of acetylcholine, is applied to the cornea. The pupillary constrictor muscle should cause miosis within 10 or 15 minutes. This drug concentration has no effect in a normally innervated eye. Abrasion of the cornea (even by use of a Schirmer tear strip in the previous few days) may allow increased uptake of pilocarpine so that normally innervated ciliary muscle will respond. However, this response is not usually as rapid in onset, profound or sustained as in a denervated eye. For comparison a control cat should also be tested. An occasional side effect of this drug is marked chemosis (oedema of the conjunctiva), but this usually reverses within 24 hours and responds well to topical corticosteroid and / or local anaesthetic.
- the prolapsed third eyelid should not normally retract in response to a 1:10,000 solution of epinephrine, unless it results from sympathetic denervation. If too strong a solution is used it will cause some change to the position of the third eyelid of a normal cat, which should again be used as a control.

Additional tests include low plasma or urine catecholamine levels and lack of response to intradermal histamine (Wise and Lappin 1990).

Differential diagnosis

A cat with cauda equina lesions, shock and dehydration due to sacral fracture following a road traffic accident, or a cat with neurological disease due to FIP, might demonstrate some of the features of feline dysautonomia. These can include urinary retention, faecal incontinence, constipation, anal areflexia, proprioceptive deficits in the pelvic limbs, and possibly prolapsed third eyelids. However, such a cat should not show any features in Group A (Table 12.3) and further evaluation should define the true cause of the clinical signs.

FeLV-associated tonic pupils, which may be accompanied by urinary incontinence (Barsanti and Downey 1984), appears to be a distinct clinical entity. There is no specific association of feline dysautonomia with FeLV. The FeLV-associated urinary incontinence is mild and consists of leakage during sleep with otherwise normal bladder emptying, whereas in feline dysautonomia there is usually marked bladder atony. Also, the pupils in feline dysautonomia are fixed while in FeLV associated anisocoria they usually undergo a rapid spontaneous change in diameter over a short period of time.

Treatment

In the initial stages some severely affected cats will be hypoglycaemic and hypovolaemic with electrolyte disturbances, which must be corrected by intravenous fluid therapy. Metaclopramide may reduce vomition. Regurgitation should be countered by aspiration of oesophageal contents by oral or nasogastric intubation, in order to lessen the risk of pneumonia. External provision of heat is important as thermoregulation is disturbed in dysautonomia. Steam inhalation is reported to aid oronasal and lacrimal secretion. Gentle glycerol and liquid paraffin enemas to counter constipation are helpful, and cleansing of the perineal area combined with general grooming improves the cat's demeanour. Manual evacuation of an atonic bladder is vital, even though dysautonomic cats may be seen to squat and make frequent attempts to pass small amounts of urine. If there is any evidence of respiratory or urinary tract infection, antibiotics should be administered. Total parenteral nutrition has been used successfully for short term management (Canton and Sharp 1988).

After initial stabilisation, feeding by nasogastric or gastrostomy tube is preferable in cats with marked oesophageal dysfunction. Food given by tube needs to be liquidised and a small amount of Isogel® bulk laxative should be mixed in. If gastric contents are vomited, metoclopramide may again prove valuable. The technique for percutaneous gastrostomy intubation works well, but does require an endoscope (Matthews and Binnington 1986). The cat must be anaesthetised to perform this procedure, but once the tube is in place it can be managed successfully for months. Nasogastric intubation, following local anaesthetic spraying of the nares, is also well tolerated (Rochlitz 1984). Pharyngostomy intubation has been unsuccessful in most cases, although it was helpful in one cat with good gastric emptying (Sharp *et al* 1984).

Later on, oral intake of food can be attempted starting with aromatic meals. This will be aided by postural management such as by nursing the cat after feeding in an upright position for as long as possible. Diazepam, corticosteroids or progestagens can be tried as short term appetite stimulants, although the last two are catabolic in the long term. Anabolic steroids may be helpful. Regular attention to bladder evacuation, and management of defecation and hydration status are vital. Much of the longer term nursing must be performed by the owner. Adequate counselling regarding the time commitment, the likely recovery period, and the failure and complication rates, are vital on initial diagnosis so that the owner can reach a rational decision.

Autonomic stimulants, such as pilocarpine 0.1-0.5% or physostigmine 0.5% eye drops, may aid oronasal and lacrimal secretion and the latter given 20 minutes before feeding may stimulate oesophageal function. However, these drugs can induce both muscarinic and nicotinic side effects such as abdominal cramps and muscular fasciculations. Bethanechol (total daily dose 2.5 mg to

7.5 mg, divided BID or TID), may promote useful glandular, bowel and bladder function but should not be used with other stimulants. Danthron (Riker Laboratories) poses less of a problem when combined with other parasympathomimetics and is used at 1-5 ml of a 5 mg/ml solution orally per day. Metoclopramide (0.1 mg/kg IV) is a dopamine antagonist which has been documented to show fluoroscopic improvement in gastric emptying in dysautonomia (Canton and Sharp 1988). This drug can cross the blood brain barrier to cause excitation. However, its potential benefits to gastric feeding of a cat with ileus are obvious.

Histopathology

This feature has been well described elsewhere (Sharp *et al* 1984; Griffiths *et al* 1985). Both sympathetic and parasympathetic divisions of the autonomic nervous system are equally affected. The light and electron microscopic appearance of affected neurones is pathognomic for feline and canine dysautonomia.

Prognosis

The grading system in Table 12.3 can also be used to gain some prognostic information. In general cats with Grade 3 or 4 clinical signs have a worse prognosis than those with grades 1 or 2, which is supported by the recent higher survival rate (Baxter and Gruffydd Jones 1987). However, cats of grade 4 severity can survive long term. They often show residual signs such as dilated pupils, low body weight, occasional regurgitation and are likely to be less tolerant of severe stress. One cat recovered well from a grade 4 presentation, but at five months went into a profound state of cardiovascular and physiological collapse following a routine radiological examination, and died within two hours (Canton and Sharp 1988). Cats have occasionally developed more unusual neurological signs after apparent recovery. Some mildly affected cases of grade 1 or 2 have made good progress but then developed faecal incontinence necessitating their euthanasia as late as nine months after the initial onset of illness.

Canine Dysautonomia

Cases have been described to date from both the United Kingdom, Europe and the USA (Pollen and Sullivan 1984; Wise and Lappin 1990). Dysuria, diarrhoea, and loss of the anal reflex seem to be a common features. The clinical picture is very reminiscent of feline dysautonomia and the histopathology shows identical changes to the feline disorder.

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CHAPTER THIRTEEN

Episodic Weakness and Collapse

Michael E. Herrtage and Rosemary E. McKerrell

INTRODUCTION

Many neurological disorders are episodic in nature, for example, seizures in idiopathic epilepsy, and recurrent paraparesis in thoracolumbar disc disease. Generally, these are well recognised entities, and are covered elsewhere in this Manual. However, there are a number of less well defined conditions, which show episodes of weakness, neurological deficits or behavioural disturbances. Also, there are other conditions in which the signs may vary considerably throughout the course of the condition, giving the impression of an episodic occurrence. This chapter aims to assist the clinician in the differential diagnosis of these disorders, and whilst not all conditions in this chapter invariably present as episodic weakness and collapse, some have been included because they may at times cause confusion.

Episodic weakness is a prominent clinical sign in a large variety of diseases. It can be defined as a waxing and waning weakness interspersed with periods of apparent normality. The degree of weakness may vary from mild pelvic limb ataxia, to total collapse or syncope.

Syncope or fainting is defined as a sudden, brief loss of consciousness. It is caused by a temporary lapse in cerebral function, usually as a result of reduced cerebral blood flow, inadequate oxygen delivery or inadequate glucose availability. Syncopal episodes are most frequently seen with cardiovascular, respiratory, metabolic or endocrine abnormalities. The same pathophysiological mechanisms may cause episodic pelvic limb weakness or ataxia, but other conditions, for example, neuromuscular disorders, can also produce these clinical signs.

Primary neurological disorders, for example seizures, can cause syncopal-like signs. These require careful investigation to differentiate them from true syncope. A seizure, which is a period of abnormal behaviour caused by a sudden, abnormal and excessive electrical discharge from the brain, frequently occurs in three stages; the prodromal phase, the actual seizure or ictal phase and the post-ictal phase. This latter phase can sometimes be particularly difficult to differentiate from other causes of episodic weakness or syncope. In general, however, there are no prodromal signs and few post-ictal repercussions with other causes of episodic weakness or syncope. A detailed discussion of seizures can be found in Chapter 7; only the major differential points will be mentioned in this chapter.

The differential diagnosis of episodic weakness presents a major diagnostic challenge to the clinician. Most of the patients appear normal when they are initially presented to the veterinarian, thus meticulous attention to the information contained in the signalment, history and physical examination is important. Access to routine and sometimes specialised diagnostic aids is usually necessary to confirm a diagnosis.

DIAGNOSTIC APPROACH

A list of some of the conditions that may be associated with episodic weakness is presented in Table 13.1. The differential diagnosis is extensive, and thus a logical and thorough investigation is essential if a diagnosis is to be made. A sequential diagnostic approach is given in Figure 13.1.

Signalment

Certain breeds are associated with diseases which cause episodic weakness (Table 13.1; see also Appendix 1). However, some breeds are associated with more than one condition and the association is by no means exclusive. Age and sex may limit the diagnostic possibilities or increase the index of suspicion in certain conditions.

History

An accurate and detailed history is critical to the eventual diagnostic success of a case. Questions concerning the episodes of weakness are of paramount importance, because the veterinarian may never actually witness an episode. Many observant owners can relate sufficient information to allow the clinician to reduce the number of possible differential diagnoses. A detailed description of the episode should be gleaned from the information provided in the answers to the following questions:

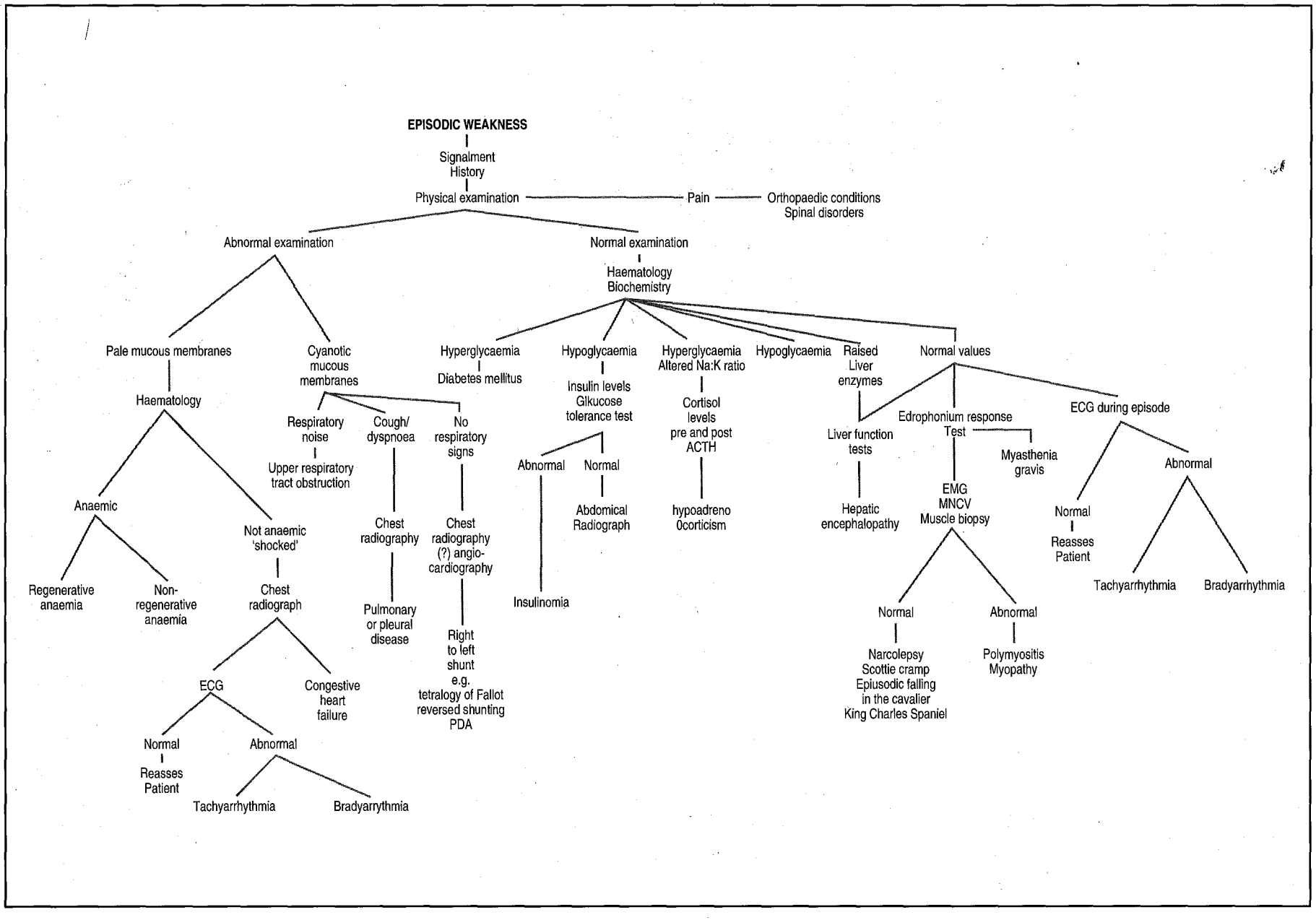

Figure 13.1: Sequential diagnostic approach.

Table 13.1: Differential diagnosis of episodic weakness

Cardiovascular disorders
- Bradyarrhythmia
- Tachyarrhythmia
- Congenital heart disease eg. aortic or pulmonic stenosis, tetralogy of Fallot, reverse-shunting PDA
- Acquired heart disease eg. valvular, myocardial, pericardial
- Heartworm disease (Dirofilariasis, Angiostrongylosis)
- Vasovagal syncope
- Vasodilation
- (Aortic) thromboembolism

Respiratory disorders
- Laryngeal paralysis
- Upper respirator tract obstruction, especially brachycephalic breeds
- Tracheal collapse
- Severe coughing
- Filaroides osleri
- Pulmonary disease
- Pleural effusions
- Thoracic masses

Haematological disorders
- Anaemia - regenerative eg. ruptured splenic haemangiosarcoma
  - non-regenerative
- Myeloproliferative disorders
- Polycythaemia
- Hyperviscosity syndrome
- Haemoglobinopathies
- Pyrexia of unknown origin

Orthopaedic disorders
- Degenerative joint disease particularly hips or stifles
- Polyarthritis - various types

Neurological disorders
- Congenital or acquired spinal disorders, including Wobbler syndrome
- Epilepsy (various causes)
- Vestibular disease
- Cerebellar disorders
- Thiamine deficiency
- Congenital disorders eg. hydrocephalus
- Acquired disorders eg. old dog encephalitis, tumours
- Lysosomal storage diseases
- Giant axonal neuropathy
- Progressive axonopathy - Boxer
- Tetanus
- Botulism
- Narcolepsy/cataplexy - Dobermann, Poodle, Labrador retriever
- Generalised tremor
- Jack Russell ataxia
- Scottie cramp - also seen in the Norwich terrier, Dalmatian and Jack Russell terrier
- Episodic falling in the Cavalier King Charles spaniel .

Neuromuscular disorders
- Myasthenia gravis
- Polymyositis
- Hereditary myopathy of Labrador retrievers
- Hereditary myopathy of Devon rex cats
- Sex-linked muscular dystrophy - Irish terriers, Golden retrievers
- Myotonia in chow chows, Staffordshire terriers
- Feline hypokalaemic polymyopathy
- Ischaemic neuropathy due to thromboembolism
- Malignant hyperthermia
- Mitochondrial myopathies eg. pyruvate dehydrogenase deficiency
- Exertional myopathy (rhabdomyolysis)

Metabolic disorders
- Hepatic encephalopathy - portosystemic shunts, cirrhosis
- Uraemic encephalopathy
- Hyperglycaemia
- Hypoglycaemia
- Hyponatraemia
- Hyperkalaemia
- Hypokalaemia
- Hypercalcaemia
- Hypocalcaemia
- Hypermagnesaemia
- Hypomagnesaemia
- Acidosis
- Hyperthermia (heatstroke)
- Hypoxia
- Shock

Endocrine disorders
- Insulinoma
- Hyperadrenocorticism (Cushing's disease) myotonia
- Hypoadrenocorticism (Addison's disease)
- Hypoparathyroidism
- Hypothyroidism
- Phaeochromocytoma
- Diabetic ketoacidosis

How many episodes has the animal suffered?

Do the episodes follow a similar pattern?
Seizures and syncopal attacks tend to follow the same pattern on each occasion, whereas in most of the metabolic disorders, the clinical signs vary from episode to episode.

What time of the day do the episodes occur?
In idiopathic epilepsy, the seizures usually occur when the animal is at rest, or on waking.

Are there any associations with the onset of an episode?
Weakness following excitement, exercise or stress is often associated with cardiovascular and neuromuscular disorders. The amount of exercise that causes weakness or collapse may be fairly constant and predictable, as in myasthenia gravis, or it may be variable, as in episodic falling in the Cavalier King Charles spaniel. Metabolic disorders are not usually associated with exertion.

There may be a relationship to feeding. In hypoglycaemia, episodes occur either after fasting or just after eating. Feeding may also precipitate signs of hepatic encephalopathy, particularly if the food has a high protein content.

Seizures are often preceded by a prodromal phase (aura), which is characterised by a change in either behaviour (nervousness), or motor function (head turning or focal muscle twitching).

Does the animal lose consciousness?
With peripheral neuromuscular disorders, the animal will be totally aware of its surroundings, and its eyes will tend to follow the owner. In contrast, animals with seizures usually lose consciousness. Metabolic and endocrine disorders vary in severity, but in cases severe enough to cause collapse, the animal will be depressed with occasional loss, or apparent loss, of consciousness. In cardiovascular disorders, the animal may be collapsed, dazed or unconscious.

What does the animal do during the actual episode?
The clinical expression of seizures varies depending on the area of the brain affected. Generalised motor seizures are usually characterised by symmetrical involvement of the entire body with tonic /clonic movements of the limbs and jaws, body tremor, loss of consciousness, salivation, tachypnoea, tachycardia, urination and defecation. Syncope usually produces a flaccid collapse, although there may be vocalisation, stiffening of the limbs and even urination, thus requiring careful differentiation from seizures. Syncope is neither preceded by a pre-ictal period nor followed by any unusual post-ictal behaviour.

Does the owner notice any change in the colour of the mucous membrane or in heart rate?
It is important to know whether there is evidence of pallor or cyanosis of the mucous membranes, and whether the heart is beating quickly or slowly during the collapse. The owner may not be able to answer these questions initially, and it may be necessary to ask the owner to check for these signs should the animal have another episode.

How long does an episode last?
Most episodes are brief. However, owners are understandably anxious and tend to overestimate the duration of an attack. Syncope usually lasts from seconds to no more than a few minutes, whereas seizures often last from one to five minutes. With metabolic or endocrine disorders, the animal may appear dazed, confused or weak for hours before slowly recovering. Patients with myasthenia gravis collapse on exercise, rest for a few minutes then appear to recover for a short time before collapsing again.

Is the animal normal afterwards?
The post-ictal phase of a seizure may vary from a few minutes to several days. Its length is not related to the severity or cause of the seizure. The animal may be depressed or overly excited, sleep or constantly pace, and may be thirsty or hungry, or both. The clinician may be misled if the owner misses the actual seizure and only observes the post-ictal phase when the animal is ataxic and weak. It is important to enquire whether there was any sign of disturbance (e.g. to bedding, furniture, etc.) or urination, which might suggest a seizure.

From this information the clinician should be able to piece together a clear impression of the episode. Although most animals appear normal between episodes, it is still important to ask about the general health of the patient. In hypoadrenocorticism, for example, the animal may show anorexia, weight loss, gastrointestinal upsets, polydipsia and polyuria even between bouts of weakness. In every case, information should be gained about appetite, thirst, urination, weight loss or, in young animals, failure to thrive, vomiting, diarrhoea and exercise tolerance.

Physical Examination

A complete physical examination, including a full neurological assessment should be carried out in every patient, even if the clinician feels there are limited diagnostic possibilities. Animals with pain or discomfort caused by orthopaedic or spinal conditions may be reluctant to move or incapable of walking normally, and the owner may incorrectly assess this as weakness. Most of these animals will still be experiencing pain when they are examined.

Clinical experience, history and physical examination may allow the clinician to differentiate or characterise the disorder so that only confirmation of the diagnosis is required. However, many cases of episodic weakness require careful and logical investigation to confirm the

cause. This is particularly true when no abnormalities are found on physical examination. Further investigation will require some or all of the examinations discussed below.

Laboratory Tests

Routine haematology and a biochemical profile including electrolytes (sodium, potassium, calcium and magnesium), blood glucose, urea, liver enzymes (ALT, ALP) and muscle enzymes (CK, AST) should be considered the minimum data base. Interpretation of these results with respect to episodic weakness is given in Table 13.2. (See also Chapter 4).

In some cases the minimum data base will provide the diagnosis, but in other patients further laboratory investigations are indicated.

Table 13.2: Interpretation of laboratory findings with respect to episodic weakness.

HAEMATOLOGY		
Anaemia -	regenerative	
	non-regenerative	
Polycythaemia		
BIOCHEMISTRY		
Blood urea	high -	renal failure
		hypoadrenocorticism
	low -	hepatic encephalopathy
		hyperadrenocorticism
Blood glucose	hyperglycaemia -	diabetic ketoacidosis
		hyperadrenocorticism
	hypoglycaemia -	insulinoma
		neonatal puppies
		toy and miniature breeds of dogs
		working/hunting dogs
		septicaemia
		nonpancreatic tumours (especially hepatocellular carcinomas)
		liver disease
		hypoadrenocorticism
		excess insulin therapy
Sodium	hyponatraemia -	hypoadrenocorticism
Potassium	hyperkalaemia -	hypoadrenocorticism
		acute renal failure
		diabetic ketoacidosis
		severe acidosis
	hypokalaemia -	urinary loss (especially cats with hypokalaemic polymyopathy)
		severe vomiting and/or diarrhoea
		excessive fluid therapy
		insulin administration
Calcium	hypercalcaemia -	hypoadrenocorticism
		primary renal failure
		certain malignancies
		lymphosarcoma
		anal gland adenocarcinoma
		bone metastases
		primary hyperparathyroidism
	hypocalcaemia -	postparturient eclampsia
		hypoparathyroidism
		terminal renal failure
		protein-losing enteropathy
		severe alkalosis

Liver function tests

When hepatic encephalopathy is suspected, liver function tests should be performed. Serum bile acid determinations are very sensitive indicators of portosystemic shunting and hepatobiliary disease, and have tended to replace bromsulphthalein (BSP) retention and ammonia tolerance tests. Fasting bile acid concentrations are usually sufficient, but pre- and postprandial sampling is even more accurate.

Adrenocortical function tests

An ACTH stimulation test is necessary to confirm the diagnosis of hypoadrenocorticism. It is also a useful screening test for hyperadrenocorticism. The low-dose dexamethasone test has some advantages over ACTH stimulation in screening for hyperadrenocorticism, but it is not as useful in the detection of iatrogenic Cushing's disease and is affected by more variables. The high-dose dexamethasone test is used to differentiate adrenal-dependency from pituitary-dependency in hyperadrenocorticism, if this has not already been determined.

Other hormone estimations

If hypothyroidism is suspected, a basal thyroxine (T4) assay should be performed preferably followed by a TSH or TRH stimulation test. Insulin assays may be useful in cases of functional pancreatic islet cell tumour (insulinoma).

Immunological tests

In some of the immune-mediated disorders, immunological tests may provide useful information. For example, tests for antinuclear antibody (ANA) may be positive in cases of polymyositis, and antibodies to acetylcholine receptors are diagnostic of acquired myasthenia gravis.

Blood gas and acid-base estimations

Blood gas analysis provides values for plasma pH, pCO_2 and pO_2, and these can be used to calculate bicarbonate and base excess concentrations. Arterial or venous blood samples can be used to evaluate pCO_2 and base excess concentrations, but oxygen concentrations are only meaningful on arterial samples. In cases of episodic weakness, pre- and post-exercise samples are usually required to aid the diagnosis. Blood gas analysis may be useful in obstructive pulmonary disease, upper respiratory tract obstruction, right to left cardiac shunts, diabetic ketoacidosis, and mitochondrial myopathies. Pre- and post-exercise blood lactate and pyruvate determinations may also prove useful, particularly in the assessment of muscle disorders.

Cerebrospinal fluid analysis

Examination of CSF is justified in some patients with episodic disorders (see Chapter 4).

Radiology

Thoracic radiographs are useful for ruling out significant cardiopulmonary disease. Particular attention should be paid to the shape and size of the cardiac silhouette and the clarity and radiological pattern of the lung fields. If tracheal collapse is suspected, both inspiratory and expiratory lateral radiographs are required to demonstrate cervical and intrathoracic collapse respectively.

Radiographs of the abdomen, spine, skull and limbs may be indicated by the physical examination.

Contrast studies may be required in selected patients, for example, portal venography will identify the portosystemic shunts that cause hepatic encephalopathy, and myelography may be required to rule out some spinal conditions. Angiocardiography, usually in combination with intracardiac pressures and blood gas estimations, is necessary for defining some congenital heart defects.

Ultrasound and particularly echocardiography are useful for providing additional data in specific cases and in some patients will obviate the need for contrast studies.

Electrocardiography (ECG)

An ECG should be performed in all cases in which a cardiac cause is suspected. The rate and rhythm should be carefully assessed, because conduction abnormalities and arrhythmias are a major cause of episodic weakness and syncope.

When the arrhythmias are continuous, as in atrial fibrillation or third degree atrioventricular block, the diagnosis is relatively straightforward and may be made from a single recording. However, certain types of arrhythmia, such as premature contractions, paroxysmal tachycardias or sinoatrial block, may be intermittent. In these cases a rhythm strip should be repeated after a vagal manoeuvre such as ocular pressure or carotid sinus massage, and following exercise. Even so, the ECG is frequently normal in animals who have syncope associated with cardiac arrhythmias. In these cases, 24-hour ambulatory ECG monitoring is required to define the arrhythmia precisely (Hall *et al* 1991).

A simple device such as the Chiltern Box can be used by the owner to record an ECG at the time of the collapse (Brownlie 1987).

In some cases, adequate information regarding the arrhythmia may be obtained by simply teaching the owner how to monitor the heart rate during an episode, with a stethoscope if necessary.

Electroencephalography (EEG)

An EEG may be indicated in some cases, although it is of greater value in the diagnosis of structural rather than functional diseases of the CNS.

Electromyography and Nerve Conduction Studies

These tests are indicated for some patients with episodic weakness or collapse.

Nerve conduction

Measurement of nerve conduction is of most value in peripheral neuropathies. Repetitive nerve stimulation may reveal a decremental response in the amplitude of the evoked response recorded from the muscle in patients with myasthenia gravis, and this response can be shown to be abolished by the administration of anticholinesterase drugs.

Electromyography

Using the same equipment the electrical activity present within the muscle itself may be recorded in EMG. (See Chapter 4)

Muscle and Nerve Biopsies

(See Chapter 4).

Edrophonium Response Test

Edrophonium chloride (Camsilon®, Cambridge Laboratories. Drug formerly available as Tensilon®) is an ultra-short acting anticholinesterase used in the diagnosis of myasthenia gravis. A dose of between 0.1 mg and 1.0 mg, depending on the size of the animal, is given by slow intravenous injection. Oxygen should be available in case respiratory difficulty occurs. In patients with myasthenia gravis, administration of edrophonium produces a dramatic improvement in ability to exercise, which is observed almost immediately and lasts for several minutes. Care should be taken over the interpretation of the test as occasionally there may be some non-specific improvement in other neuromuscular disorders. This test is of particular value in the investigation of episodic weakness characterised by fatigue on exercise.

SPECIFIC CONDITIONS

Cardiovascular Disorders

Cardiac causes of episodic weakness and / or syncope are associated with either reduced cerebral blood flow or inadequate oxygen delivery to the brain (Beckett *et al* 1978).

Cardiac rhythm disturbances

Severe supraventricular or ventricular tachyarrhythmias, or severe bradyarrhythmias including third degree AV block or sinus node disease. The episodes are most commonly associated with exercise or excitement, but may occur at rest if the arrhythmia is severe. The diagnosis can only be confirmed by ECG.

Ventricular outflow obstruction

Aortic stenosis, pulmonic stenosis, hypertrophic cardiomyopathy, and heartworm disease are possible causes. Outflow obstruction is usually associated with a systolic murmur, and limits the overall ability of the ventricles to maintain cardiac output especially during exercise or excitement. Cardiac arrhythmias may complicate the situation. Diagnosis is dependent on physical examination, ECG, radiography and cardiac catheterisation. Echocardiography is helpful and may obviate the need for invasive procedures such as cardiac catheterisation.

Heart failure

An inability to sustain forward flow is frequently observed in dilated cardiomyopathy and in severe mitral insufficiency. Pulmonary oedema may also lead to inadequate oxygen uptake. Under these circumstances exercise and excitement are most likely to cause episodic weakness and / or syncope. The diagnosis can be made on physical examination, radiography and ECG, but echocardiography can provide useful information about chamber size and contractility.

Cardiac tamponade due to pericardial effusion

Causes include neoplasia (haemangiosarcoma, heart base tumours), idiopathic, left atrial rupture, trauma, infection, chronic uraemia and right-sided heart failure. Pericardial effusion results in increased intrapericardial pressure, once the elastic limit of the pericardial sac has been exceeded. This pressure on the myocardium impairs normal diastolic filling of the heart. Inadequate ventricular filling results in a reduction in cardiac output with consequent signs of weakness and syncope. Weakness or syncope are rarely the sole presenting signs; hepatomegaly, ascites and dyspnoea are usually present as well. Although radiography and ECG can provide useful information, echocardiography is the most sensitive and specific means of diagnosis.

Right-to-left shunts

Weakness or syncope usually occur with exercise when lowered peripheral resistance increases the amount of deoxygenated blood shunted into the systemic circulation. Tetralogy of Fallot and reverse-shunting patent ductus arteriosus are examples. In the latter case there is usually no murmur, and the pelvic limbs are more affected because of the anatomical position of the patent ductus arteriosus.

Vasodepressor or vasovagal syncope

This is poorly understood in animals, but probably explains some cases of syncope in brachycephalic breeds particularly the boxer. Syncope is caused by an increase in vagal tone, which causes transient and usually profound bradycardia.

Cardiac drugs

Overzealous use of diuretics (e.g. frusemide) that reduce plasma volume, or vasodilators (e.g. hydralazine, prasozin, enalapril and captopril) that produce hypotension can cause weakness or syncope, particularly when they are used in combination.

Respiratory Disorders

Respiratory causes of episodic weakness and / or syncope are usually associated either with inadequate oxygen delivery to the brain or with reduced cerebral blood flow. Hypoxaemia can result from any form of respiratory tract obstruction, or any disease process that reduces lung capacity or interferes with oxygen uptake. Episodic weakness and / or syncope from hypoxaemia is seen most commonly with laryngeal paralysis, upper respiratory tract obstruction in brachycephalic breeds, and tracheal collapse. These conditions are associated with upper respiratory tract noise and coughing. Pleural effusions, intrathoracic masses and diffuse pulmonary disease can also lead to hypoxaemia. In all of these conditions, episodic weakness and collapse will usually follow a period of exercise, excitement or stress.

Severe coughing of any cause may result in episodic weakness and syncope by reducing cerebral blood flow. During coughing, the intrathoracic pressure is markedly elevated causing a severe reduction in venous return to the heart. Cardiac output is reduced thus decreasing cerebral blood flow. Weakness or syncope occurs at the end of a bout of coughing.

History, physical and radiological examinations, and blood gas analysis are useful in diagnosing respiratory causes of episodic weakness and collapse. In some cases, endoscopy of the upper and lower respiratory tract will be required to make a diagnosis.

Haematological Disorders

Severe anaemia and sudden haemorrhage can give rise to hypoxaemia severe enough to cause weakness and collapse. In most cases, the weakness and collapse are associated with exercise, excitement or stress. In some, however, the clinical signs follow sudden and / or recurrent haemorrhage, for example, a ruptured splenic haemangiosarcoma (Brown *et al* 1985).

Polycythaemia is a rare cause of episodic weakness and collapse, which is thought to occur because increased viscosity of the blood and increased vascular resistance result in reduced cerebral perfusion. These signs are precipitated by exercise and exertion. Hyperviscosity may also be seen with monoclonal gammopathies such as multiple myeloma, lymphocytic leukaemia, and lymphosarcoma.

Pyrexia of unknown origin may also cause episodic weakness and collapse. The differential diagnosis of pyrexia of unknown origin, which includes the broad categories of infection (systemic or localised), neoplasia, immune-mediated disease and miscellaneous causes, has been reviewed elsewhere (Dunn and Gorman 1987).

PRIMARY CENTRAL NERVOUS SYSTEM DISORDERS

Most of the central nervous causes of episodic weakness and collapse listed in Table 13.1 are covered elsewhere in this Manual. Particular attention should be taken to differentiate seizures from other causes of episodic weakness and collapse. Narcolepsy / cataplexy complex, Scottie cramp and episodic falling in the Cavalier King Charles spaniel will be dealt with here in more detail.

Narcolepsy / Cataplexy Complex

Narcolepsy is a disorder of sleep, characterised by episodic sleepiness at inappropriate times. Cataplexy, the most common sign in animals, is characterised by sudden paroxysmal attacks of flaccid paralysis, which may last from a few seconds to several minutes. The attacks are most commonly associated with excitement from eating or playing and may be reversed by petting or calling the animal's name. The respiratory and ocular muscles tend to be spared.

Narcolepsy / cataplexy has been reported in many breeds (Mitler *et al* 1976). It is believed to be an autosomal recessive condition in Dobermanns, and is thought to be inherited in Poodles and Labrador retrievers. Diagnosis is based on the clinical signs, which can be induced by exercise or feeding. Signs are usually present before six months of age, although adult dogs may develop the disease. During an attack, the animal is usually in sternal or lateral recumbency, and appears unconscious and limp. There may be twitching of the eyelids, whiskers and paws, but there is no salivation, urination or defecation.

The disease is not life threatening and does not usually progress with time. Animals may respond favourably to imipramine (Tofranil®) at a dose of 0.5 - 1.5 mg/kg orally BID or TID.

Scottie Cramp

This is an inherited condition of Scottish terriers, which usually presents between six weeks and 18 months of age (Joshua 1956; Meyers *et al* 1969). At rest the dog appears normal but after a variable amount of exercise the thoracic limbs are abducted, the back becomes arched and the pelvic limbs appear to hyperflex. As the muscular tone increases the dog may fall over, curl into a ball and apparently stop breathing. There is no loss of consciousness and recovery usually begins after about 15 seconds. Attacks appear to be precipitated by anxiety and excitement, and the frequency and severity varies between individuals.

Episodes may be induced by administration of serotonin antagonists, such as methysergide (Deseril®). The drug is given orally at a dose of 0.3 mg/kg and the

dog is then exercised two hours later. The underlying cause of the disease is not fully understood, but it appears to be due to a disorder of neurotransmission in the CNS, probably a defect in the serotonergic neurons. Chlorpromazine, acepromazine and diazepam are effective in suppressing the clinical signs.

A similar condition has been described in the Dalmatian, in one Jack Russell terrier and more recently a form of "cramp" has been reported in Norwich terriers (Furber 1984). In affected Norwich terriers spasms of the muscles of the hindquarters lasting approximately five minutes may occur during or after exercise. The condition has apparently been recognised for some years by breeders, who have suggested that dietary supplementation with seaweed or selenium may reduce the incidence.

Episodic Falling in the Cavalier King Charles Spaniel

This condition has been recognised by breeders for many years. The age of onset varies from three months to four years (usually three to four months), and episodes may be triggered by stress or excitement (Herrtage and Palmer 1983). After a variable amount of exercise a bounding gait develops. The back is arched and the dog may "bunny hop". The pelvic limbs are abducted and appear stiff, although muscle tone is unaltered during attacks. The thoracic limbs may show excessive protraction to the extent that, when the animal collapses, the thoracic limbs are held crossed over the back of the head. During the collapse there is no loss of consciousness and recovery is rapid. There is no response to edrophonium chloride, and the anticonvulsant drug, carbamazepine (Tegretol®) may increase the frequency of the episodes. No abnormalities have been detected on either routine haematology, biochemistry or in either of the two affected animals on which post mortem examinations have been carried out. Episodic falling may be associated with "fly-catching", and bears some resemblance to Scottie cramp in which there is thought to be a functional defect in serotonergic neurons.

Treatment with diazepam may give some improvement, but usually this is not permanent.

NEUROMUSCULAR DISORDERS

Neuromuscular disease is being recognised more frequently in veterinary practice as the conditions become more clearly defined. Neuromuscular causes of episodic weakness and collapse include peripheral neuropathies, disorders of neuromuscular transmission, and myopathies. Peripheral neuropathies are dealt with in Chapter 14.

Myasthenia Gravis

Myasthenia gravis is a disorder of the neuromuscular junction which has been reported in both dogs and cats. In dogs, acquired and congenital forms of myasthenia are recognised (Palmer 1980).

Acquired canine myasthenia gravis

Most cases of generalised acquired myasthenia gravis are seen in adult dogs of large breeds, especially German shepherd dogs. The condition occurs as a result of the production of antibodies to acetylcholine receptors, which destroy the neuromuscular junction. Acquired myasthenia is therefore considered to be immune-mediated and may be found in association with the presence of a thymoma (Aronsohn *et al* 1984).

Signs are of severe muscular weakness, particularly of the thoracic limbs, and fatigue on exercise which improves with rest. The stride is short and, as the dog tires, the head is progressively lowered until eventually the dog refuses to continue or collapses. The condition is frequently associated with dysphagia and regurgitation related to megaoesophagus, which can be seen on thoracic radiographs. Involvement of the oesophagus occurs in this condition because of the high proportion of striated muscle present in the canine oesophagus. Recently a focal form of acquired myasthenia has been reported in which regurgitation was the principal sign, although some dogs with this form of the disease also had weakness of the pharyngeal, laryngeal and / or facial muscles. In a study of 152 dogs with idiopathic acquired megaoesophagus, 40 dogs had positive antibody titres to acetylcholine receptors and 48 per cent of these showed clinical improvement or remission of clinical signs associated with decreasing antibody titres (Shelton *et al* 1990).

Diagnosis of acquired myasthenia gravis is based on clinical signs and on the response to anticholinesterase drugs (see "Edrophonium response test" above). Affected dogs show a dramatic improvement on administration of edrophonium, which lasts for several minutes. Repetitive nerve stimulation may demonstrate a decremental response in the amplitude of the evoked response recorded from the muscle, but this is seldom necessary for diagnosis. The diagnosis can also be confirmed by the demonstration of autoantibodies to muscle acetylcholine receptors and is required to diagnose the focal form of the disease.

Treatment consists of the oral administration of longer acting anticholinesterase drugs, for example, pyridostigmine bromide (Mestinon®). The dose of pyridostigmine required varies according to the size of the dog, the severity of the signs and the response to treatment. The dose may therefore range from 7.5 mg orally once a day in a Jack Russell terrier, to 60 mg two or three times daily in a German shepherd dog. The edrophonium response test can also be used to determine whether a myasthenic patient is receiving inadequate or excessive treatment with cholinergic drugs. This is important because both will manifest as weakness, and inadvertent overdose of anticholinesterase may prove fatal. If anticholinesterase treatment is

excessive an injection of edrophonium will either have no effect or will intensify the signs (oxygen should be available in case of respiratory arrest). Conversely, transient improvement will be seen if the patient is being inadequately treated.

As acquired myasthenia is immune-mediated immunosuppressive levels of glucocorticoids (2 mg/kg prednisolone BID) may be beneficial. However care must be taken when using glucocorticoids in combination with anticholinesterase drugs, as muscle weakness may be enhanced, and it is particularly important that glucocorticoids are not given if the patient shows clinical signs of inhalation pneumonia.

Some patients go into spontaneous remission and make a full recovery, but owners should be warned of the possibility of complications such as inhalation pneumonia and of the various problems which can be associated with treatment. Thymectomy should be considered in those cases where a thymoma is found.

Congenital canine myasthenia gravis

Congenital myasthenia gravis is seen in Jack Russell terriers, Springer spaniels and Smooth-haired fox terriers, and is thought to be inherited as an autosomal recessive trait. Signs of weakness are first noticed at 6-8 weeks of age. Affected pups have difficulty standing or raising their heads and may be dysphagic. As in the acquired disease, diagnosis is based on the clinical picture and on the response to edrophonium. The prognosis is generally poor, although it has proved possible to keep affected dogs alive for more than two years using small doses of oral anticholinesterase preparations.

There are no circulating antibodies to acetylcholine receptors in congenital myasthenia. The condition appears to be due to a reduced number of acetylcholine receptors present in the post synaptic membrane (Oda *et al* 1984).

Myasthenia gravis in the cat

Twelve cases of myasthenia have been reported in cats (Joseph *et al* 1988; Cuddon 1989; O'Dair *et al* 1991). Of these, ten were of adult onset and appeared to be acquired. In the other two cats, signs of edrophonium-responsive weakness first became apparent at four to five months of age. In these animals no antibodies to acetylcholine receptors could be detected in the serum and it was suggested that these may represent an example of congenital myasthenia.

Myasthenic cats exhibit a stiff gait which may give the appearance of lameness. As exercise progresses, they rapidly become weak and reluctant to stand. A common presenting sign in feline myasthenia is trembling or muscle tremor, which is not a feature of myasthenia in other species and may lead to confusion in diagnosis. Dysphagia, salivation, changes in the voice and facial weakness may also occur. Feline myasthenia has been diagnosed in association with the presence of a thymoma (Herrtage and McKerrell personal observation; Scott-Moncrieff *et al* 1990), and a cystic thymus (O'Dair *et al* 1991).

The principles of treatment are similar to the dog.

Polymyositis

Polymyositis is a diffuse inflammatory disease of skeletal muscle. Adult dogs of either sex and of any breed may be affected, although it is more common in large breeds of dogs. Presenting signs are variable, including weakness, which may appear to be episodic, fatigability, difficulty swallowing, lameness or stiffness and generalised muscle atrophy. About one third show signs of pain on palpation of skeletal muscles and megaoesophagus may be present (Kornegay *et al* 1980).

On neurological examination no specific abnormalities are found, but EMG may reveal fibrillation potentials, positive sharp waves and increased insertional activity. Elevated serum enzymes may be present, but because only some enzymes may be raised, CK, AST, aldolase and LDH should all be evaluated. Diagnosis is confirmed by examination of muscle biopsies, in which necrosis of muscle fibres and infiltration of muscle by plasma cells and lymphocytes are seen. An immune-mediated aetiology is likely in most patients and treatment with steroids often produces rapid improvement. However, it is important that toxoplasmosis and neosporosis are ruled out by serological testing and muscle biopsy before treatment with prednisolone (0.25 - 0.5 mg/kg TID) is started. Usually the response to treatment is dramatic, but if not, the dose should be doubled until improvement is seen and treatment continued for 5-10 days before reducing the dose gradually.

Labrador Retriever Myopathy

This inherited disease was first reported in the United States (Kramer *et al* 1976) and is widespread throughout the United Kingdom (McKerrell *et al* 1984). It has been variously described as type II muscle fibre deficiency, myotonia, muscular dystrophy and heritable Labrador retriever myopathy (McKerrell and Braund 1987). Onset of signs may occur between 8 and 12 weeks of age, although a later onset at approximately six months has also been observed. At exercise, affected puppies move with a stiff, stilted gait and an arched back. The head carriage is often low and many of the puppies show abnormalities of joint posture, such as overextended carpi or hyperflexed hocks. Exercise tolerance is reduced and in severe cases may be as little as 20 yards. As the animal tires, the stride shortens and the head is lowered until eventually the dog pitches forward onto its nose with no loss of consciousness. Considerable variation may be seen in the severity of the clinical signs both between individuals and within individuals from day to day, giving the impression that the

weakness is episodic in nature. At approximately one year of age the clinical signs appear to stabilise, although there is evidence that the pathological process continues to progress. However, exacerbations may occur if subjected to stress such as cold, anxiety, excitement or infection. Three adult cases are known to have developed megaoesophagus. Despite reduced exercise tolerance and generalised muscle atrophy, these dogs can make acceptable house pets.

The condition affects males and females of both yellow and black coat colour, and in the United Kingdom most of the cases have occurred in dogs from working strains. The condition has been shown to be inherited as an autosomal recessive trait. Clinical examination usually reveals generalised muscle atrophy and hypotonia, together with reduced or absent patellar and triceps reflexes. Administration of edrophonium has no effect, and CK concentrations are within the normal range or only moderately elevated. Diagnosis is suspected from the clinical picture and confirmed by the results of EMG and muscle biopsy. On EMG, fibrillation potentials, positive sharp waves and bizarre high frequency discharges (pseudomyotonic) have been observed. The pathological change in the muscle is variable, ranging from changes indicative of mild denervation to those more suggestive of primary myopathic disease.

Devon Rex Myopathy

An hereditary myopathy has been reported in the Devon rex cat (Malik *et al* 1993) and appears to be identical to the so-called spasticity syndrome, which has been recognised in this breed for some years, but in which the aetiology has remained obscure. The condition is inherited as an autosomal recessive trait.

Clinical signs are apparent from as early as 3 weeks of age and include ventroflexion of the head and neck, dorsal protrusion of the scapulae and more generalised muscle weakness, particularly following exertion, stress or excitement. Cats deteriorate up until six to nine months of age, after which the disease becomes stable or only slowly progressive. The degree of weakness is variable and may fluctuate from day to day. Megaoesophagus can be identified on thoracic radiographs, and in the cat this suggests some smooth muscle involvement. Although regurgitation is not a feature, affected cats may have problems swallowing and a number of cats have died due to laryngospasm following pharyngeal or laryngeal obstruction with food.

Serum CK concentrations are not raised in this condition. On EMG, sparse fibrillation potentials and positive sharp waves may be detected in affected muscles. Histological findings from affected muscles include variability in fibre size, hypertrophy and atrophy of fibres, rounded and split fibres, internal nucleation, individual myofibre necrosis, regeneration and fibrosis.

X-linked Muscular Dystrophy

A degenerative myopathy has been reported in Golden retrievers in the United States of America (Meier 1958; Valentine *et al* 1986; Kornegay 1988), and breeding studies have shown it to be inherited as an X-linked (males only) recessive trait. The demonstration that the muscle protein "dystrophin" is absent from the muscles of affected golden retrievers, confirmed that this disease is analogous to Duchenne muscular dystrophy of man (Cooper *et al* 1988) and represents a genuine example of canine muscular dystrophy.

Clinical signs are apparent by 6-8 weeks of age, although pathological changes may be present in the muscles from birth. Affected puppies tire quickly and develop an abnormal shuffling gait, characterised by short stiff strides. They may show reduced ability to open their jaws and difficulty in eating. The condition progresses gradually and there is considerable variation in the severity of clinical signs. Most skeletal muscles are atrophic, but hypertrophy has been observed in some muscle groups and in the tongue. Gross hypertrophy of the tongue has been reported as early as 10 days of age resulting in an inability to feed and respiratory difficulties (Meier 1958). Affected dogs show no neurological deficits and spinal reflexes are normal. Congestive heart failure due to cardiac involvement may occur.

Serum CK is greatly elevated in cases of muscular dystrophy and may also be raised in clinically normal carrier females. Values greater than 15,000 IU/l have been reported in affected dogs. With EMG, positive sharp waves and bizarre high frequency discharges (pseudomyotonic) are recorded.

Histological findings from affected muscles include fibre size variation, large rounded hyaline fibres, necrosis, phagocytosis and mineralisation with some signs of regeneration (Valentine *et al* 1986). Many of the features of this condition are identical to those of an X-linked degenerative myopathy, described previously in a litter of Irish terriers puppies (Wentink *et al* 1972, 1974). No further cases of Irish terrier myopathy have been reported, but it seems certain that the condition is identical to Golden retriever myopathy.

X-linked muscular dystrophy with dystrophin deficiency has also been reported in cats (Carpenter *et al* 1989).

Myotonia

Myotonia is characterised by the delayed relaxation of skeletal muscle following voluntary contraction or stimulation, and has been reported in man, goats, horses and dogs (Griffiths and Duncan 1973; Farrow and Malik 1981). A condition resembling myotonia congenita, an inherited condition of man, has been described in both Chow chows (Great Britain, United States, Australia, New Zealand and Holland) and Staffordshire terriers (United States) (Shires *et al* 1983). Signs first become apparent when puppies begin to

walk. Affected animals have difficulty in rising, stiffness of all four limbs, respiratory stridor and a waddling 'bunny hopping' gait. The stiffness is worse when the dog first begins to move, but improves with exercise. In some cases the generalised muscle spasm is so severe that the dog falls over and remains rigid in lateral recumbency for up to 30 seconds. Percussion of the tongue or skeletal muscles, which are usually greatly hypertrophied, results in the production of a myotonic dimple and on EMG characteristic myotonic discharges are recorded. These high frequency discharges wax and wane in both frequency and amplitude, giving rise to the so-called 'dive bomber' sound when played over the amplifier. In both the Chow chow and the Staffordshire terrier, an inherited aetiology is suspected, but the mode of inheritance has not been demonstrated.

Sporadic cases of myotonia-like conditions associated with myopathies have been reported in various other breeds, including the Cavalier King Charles spaniel (Jones and Johnstone 1982), Rhodesian ridgeback (Simpson and Braund 1985), and Great Dane (Honhold and Smith 1986).

Myotonia may also be seen in association with hyperadrenocorticism in the dog (Duncan *et al* 1977). A few affected dogs develop signs of stiffness, and hypertrophic muscles which dimple on percussion. Both myotonic and pseudomyotonic discharges may be recorded from affected muscles. These dogs also show the more classic signs of hyperadrenocorticism (see below). Diagnosis of myotonia depends on the clinical signs of stiffness, hypertrophy and dimpling on percussion, and is confirmed by EMG. Muscle biopsy may be of value in some cases.

Feline Hypokalaemic Polymyopathy

Acquired and congenital forms of this condition are recognised, and since the pathophysiology appears to be different, they will be dealt with separately. (See also Chapter 15).

Acquired hypokalaemic polymyopathy

Severe potassium depletion induces a characteristic syndrome of generalised muscle weakness in which muscle dysfunction results from the alteration in muscle cell membrane potential induced by the change in the intracellular-extracellular potassium gradient. Hypokalaemia and chronic potassium depletion is not uncommon in cats, especially older animals (Dow *et al* 1987).

Total body potassium content depends on the balance between intake and loss. Thus for depletion to occur, there must either be reduced intake of potassium or increased loss via the gastrointestinal tract or the kidneys. A retrospective study of a series of cats revealed a strong association between hypokalaemia and chronic renal disease. The mechanism by which renal dysfunction produces potassium is not fully understood and may be peculiar to cats (Dow *et al* 1989). If the loss occurs over several months, there may be severe depletion of total body potassium, particularly if the diet is in any way deficient in potassium. Hypokalaemia has also been associated with hepatic disease (Dow *et al* 1989) and profound hypokalaemia has been reported in a cat with primary aldosteronism (Eger *et al* 1983).

Affected cats develop generalised weakness with characteristic, persistent cervical ventroflexion, reluctance to move, poor exercise tolerance, and apparent muscle pain. Although the onset of signs may be acute, it has been suggested that subclinical myopathy may exist for weeks to months without obvious signs, and that hypokalaemic polymyopathy represents only the most dramatic manifestation of chronic potassium depletion (Dow *et al* 1987). Sustained hypokalaemia has also been associated with impaired renal function, weight loss, gastrointestinal disorders, lethargy and poor hair growth.

The diagnosis should be suspected in a cat with typical clinical signs and concurrent hypokalaemia (< 3.5 mmol/l and often < 3.0 mmol/l), and elevated CK concentrations (usually in the 5000 to 10,000 IU/l range). A positive response to dietary potassium supplementation is usually sufficient to confirm the diagnosis, although muscle biopsy to exclude inflammatory polymyositis may be prudent. Histological changes in hypokalaemic polymyopathy are minimal, and EMG studies usually reveal evidence of generalised sarcolemmal hyperexcitability.

Severely hypokalaemic cats should receive 8 to 10 mmol potassium/day in divided doses. A response is usually noted in 1 to 2 days, although full strength may not return for several weeks. Most affected cats require long term potassium supplementation at a dose of 2 to 4 mmol/day.

Congenital hypokalaemic polymyopathy

Hypokalaemia with a suspected hereditary basis has been described in Burmese kittens (Blaxter *et al* 1986, Jones *et al* 1988, Mason 1988). The condition is characterised by transient episodes of weakness. The onset of signs occurs between 4 and 12 months and in between attacks there may be improvement. Affected cats show weakness of the limbs and persistent ventroflexion of the head and neck, which is often accompanied by tremor or head nodding. They are reluctant to walk or jump and the gait is stiff and stilted.

Diagnosis is based on the demonstration of low serum potassium (< 3.0 mmol/l). Mild, diffuse necrosis is found in muscle biopsies, although CK concentrations may be very high (up to 97,000 IU/l). With EMG, there is increased insertional activity and the presence of positive sharp waves.

Treatment consists of a high potassium diet, but in severe cases oral potassium supplementation (5-8

mmol potassium per day in divided doses) may be required. Restoration of serum potassium to normal concentrations generally results in considerable improvement in the clinical signs, although full strength may take several weeks to return (Jones *et al* 1988).

Malignant hyperthermia

Malignant hyperthermia is a hypermetabolic disorder of skeletal muscle. It is seen most frequently in man and in pigs, but also has been reported in the dog, cat, horse and in wild animals during capture. Two precipitating mechanisms are recognised: an anaesthetic-induced form and one induced by exercise or stress, which usually affects working or sporting breeds.

In susceptible individuals the episodes of hyperthermia may be initiated by administration of certain halogenated anaesthetic agents (halothane and enflurane) and depolarising skeletal muscle relaxants (succinylcholine). The defect appears to lie in the sarcoplasmic reticulum; calcium is released but the membrane fails to take it up again leading to uncontrolled activation of muscle metabolism and sustained contraction. This results in the production of heat, acidosis, collapse, and death if untreated. In pigs the syndrome may be triggered by stress, and in one report in a Greyhound the episode came on after an anaesthetic when the dog became excited on being reunited with its owner (Kirmayer *et al* 1984).

Malignant hyperthermia may also be induced by moderate amounts of exercise (Rand and O'Brien 1987). The clinical and biochemical changes caused by exercise are conspicuously disproportionate to the intensity of the exercise. In normal dogs, exhaustive exercise (maximal heart rate for approximately one hour) is known to induce hyperlactataemia (lactate concentration increasing approximately threefold), hyperthermia (up to 41.8°C) haemoconcentration (PCV increasing 2% to 3%), and mild respiratory alkalosis. In susceptible dogs, however, these changes can occur after only a few minutes' exercise. Suspicious signs include hyperthermia (> 42°C) and hyperlactataemia (> 10 mmol/l), but before diagnosing malignant hyperthermia, other possible causes should be excluded, for example heat-stroke, pyrogens, thyrotoxic crisis, phaeochromocytoma, hypothalamic defect, drug or transfusion reaction, excessive coat or exhaustive exercise. Although the anaesthetic-induced form is often fatal, the exercise-induced form is usually reversible.

Treatment with dantrolene (Dantrium®), a muscle relaxant acting specifically on skeletal muscle, at a dose rate of 5 mg/kg intravenously is currently recommended in cases of malignant hyperthermia. Although dantrolene prevents anaesthetic-induced malignant hyperthermia, it has not been shown to prevent exercise-induced malignant hyperthermia suggesting that the latter may be initiated by a different subcellular pathway.

Mitochondrial Myopathy

Mitochondrial myopathy in Clumber spaniels was first reported by Herrtage and Houlton in 1979. Affected puppies were eager to exercise but tired quickly, sinking into sternal recumbency after approximately one hundred yards. After ten to fifteen minutes they were able to rise, but remained depressed for an hour after the collapse. During the period of collapse excessive panting and pronounced tachycardia were observed. Arterial blood samples revealed a severe acidosis after exercise, with lactate and pyruvate concentrations dramatically increased. In one animal the acidosis proved fatal. Resting concentrations of lactate and pyruvate were found to be higher than normal, and biochemical examination showed the defect to lie in the mitochondria, which were unable to oxidise pyruvate due to a deficiency in the pyruvate dehydrogenase complex. The condition has also been seen in Sussex spaniels (Houlton and Herrtage 1980) a breed closely related to the Clumber.

A single case of myopathy in which bar-like inclusions were seen in the mitochondria, was reported in a West Highland white terrier (Bradley *et al* 1988); and in 1972, Wentink *et al*, described structural and biochemical abnormalities in mitochondria from the muscles of a litter of Irish terrier puppies with an X-linked recessive myopathy (q.v.).

Exertional Myopathy

Exertional myopathy (rhabdomyolysis) is a syndrome most often seen in racing Greyhounds. There is considerable variation in both the severity of the clinical signs and the acuteness of the onset (Gannon 1980). The classic, hyperacute and acute forms of the disease are easy to recognise as the clinical signs occur during a race, but there is also a subacute form of the condition which is seen 24 to 72 hours after exercise. In these cases there is no myoglobinuria and pain is confined to the muscles of the back. Unlike the hyperacute and acute forms of the disease where mortality is high, subacute cases are not fatal and the signs are often recurrent therefore appearing to be episodic.

Predisposing factors for the condition include lack of physical fitness, a tendency to become over-excited and tense before racing, hot humid conditions, and excessive racing of fit animals.

The pathogenesis of exertional myopathy is not fully understood, and differs between the acute and subacute forms of the syndrome. The subacute form is associated with a relative potassium deficit rather than a failure of the hydrogen ion pump and alkali reserve. When the potassium concentration falls to a critical concentration, as the muscle contracts there may be insufficient outflow of potassium ions to initiate local vasodilation, causing local hyperthermia and ischaemia which result in focal necrosis of the muscle cells. Once the cell wall has lysed, myoglobin is released producing myoglobinuria. When large amounts of

myoglobin are precipitated in the kidneys, renal failure occurs and this is the usual cause of death in acute cases of the condition.

Treatment of the subacute form of the condition must take account of the fact that the underlying cause is the relative potassium deficit. The urine should be alkalinised using oral sodium bicarbonate to prevent myoglobin precipitation, and phenylbutazone given to relieve muscle pain. Anabolic steroids may also be of value.

METABOLIC DISORDERS

The differential diagnostic lists given in Tables 13.1 and 13.2 should help in the identification of specific problems. Hepatic encephalopathy will be dealt with in detail. Uraemic encephalopathy, however, is only seen in the terminal stages of renal failure when the diagnosis is usually straightforward.

Hepatic Encephalopathy

Hepatic encephalopathy is a syndrome of altered CNS function caused by hepatic insufficiency. It is seen most often in young dogs and cats with congenital portosystemic shunts, although occasionally animals with advanced liver disease and acquired portosystemic shunts will manifest clinical signs. While the exact mechanism by which these conditions induce hepatic encephalopathy remains obscure, the accumulation of toxins including ammonia, mercaptans and fatty acids is considered important. Ammonia is formed primarily in the colon by the action of urease-producing bacteria on protein and amino acids. Normally, the ammonia is absorbed into the portal vein and converted to urea in the liver. Portosystemic shunting of blood or severe hepatic disease results in excessive accumulation of ammonia in the blood, brain and CSF. Mercaptans are produced by bacterial action on methionine, which, ironically, is a constituent of some products used to treat liver disease. Short and medium chain fatty acids accumulate during hepatic failure and act synergistically with other toxins for example γ-aminobutyric acid and false neurotransmitters.

Neurological signs are variable and include depression, bizarre behavioural changes, ataxia, staggering, head pressing, circling, aimless wandering, blindness, seizures and coma. These signs usually fluctuate and are often precipitated by feeding, particularly if the food is high in protein. Other signs include stunted growth, weight loss, anorexia, vomiting, hypersalivation (particularly in cats), diarrhoea and occasionally pica. Polydipsia, polyuria, ascites and jaundice may also be present in some cases. Anaesthetic and tranquilliser intolerance may be noted.

In most cases, a biochemical profile will identify changes suggestive of liver disease. Liver enzymes, however, are usually normal in young animals with portosystemic shunts, although increased when there is active hepatic damage. Blood urea is often low, because there is decreased conversion of ammonia to urea by the diseased liver. Albumin and cholesterol may also be reduced. Confirmation of reduced liver function can be obtained from raised fasting serum bile acid concentrations. In inconclusive cases, pre- and post-prandial serum bile acid determinations, ammonia tolerance studies, or BSP excretion tests must be undertaken.

Congenital and acquired portosystemic shunts can be demonstrated by ultrasonography or by contrast radiography using operative portal venography. Liver biopsy is also useful to identify the cause of the liver disease.

Therapy should consist of a reduction in protein and fat intake, suppression or elimination of urease-containing intestinal bacteria and catharsis. Avoiding factors known to precipitate hepatic encephalopathy, for example increased dietary protein, gastrointestinal haemorrhage, excessive use of diuretics, sedatives or anaesthetic agents, uraemia, infection and constipation is considered important.

A diet high in carbohydrates and low in both fat and protein should be given. Ampicillin or metronidazole with or without lactulose may be used to control ammonia production.

Congenital portosystemic shunts have been successfully ligated, but care must be taken to check that patients have normal intrahepatic circulation after the shunt is ligated, or portal hypertension will develop with potentially catastrophic results.

Hyperglycaemia

Significant hyperglycaemia with glycosuria is seen mainly in diabetes mellitus, but it is not on its own responsible for episodic weakness and collapse except in the rare condition of non-ketotic hyperosmolar diabetic syndrome, where the blood glucose is so high (> 35 mmol/l) that it causes dehydration and shrinkage of cells especially in the brain.

Diabetic ketoacidosis in uncontrolled or poorly controlled diabetic animals is seen more frequently. Polydipsia and polyuria may have been noted previously but anorexia, vomiting, diarrhoea, profound weakness and collapse are likely to be the presenting features. Weakness and collapse is caused by hypovolaemia and acidosis.

Peripheral neuropathy related to diabetes is seen occasionally - see Chapter 14.

Hypoglycaemia

Hypoglycaemia is often caused by a functional islet cell tumour (insulinoma) in middle-aged to older dogs (see below), but may also occur with liver disease, sepsis, glycogen storage diseases and excessive insulin administration. Transient hypoglycaemia may be seen in neonatal pups, toy and miniature dogs and working dogs.

Hyperkalaemia

Hyperkalaemia increases the resting membrane potential almost to threshold, thus producing a weaker action potential when the threshold is reached. The result is muscle weakness and impaired cardiac conduction. Hyperkalaemia is found in association with hypoadrenocorticism, uncontrolled diabetes mellitus, acute renal failure and severe metabolic acidosis, but is seldom of clinical significance until the serum concentration exceeds 7 mmol/l. Higher concentrations of serum potassium are life-threatening and require immediate correction.

Hypokalaemia

Hypokalaemia increases the cellular resting membrane potential, resulting in a larger difference between the resting and threshold potential necessary for an action potential and muscle contraction. This results in difficulty in stimulating muscles to contract, producing clinical signs of muscle weakness and disturbed cardiac conduction. Hypokalaemia may result from severe vomiting, diarrhoea, urinary loss, excessive fluid therapy or insulin administration and is rarely of clinical significance until the serum concentration declines below 3 mmol/l (see also Hypokalaemic Polymyopathy above).

Hypercalcaemia

Hypercalcaemia may be associated with weakness and muscle wasting, because increased calcium concentrations decrease cell membrane permeability in nervous tissue, depressing the excitability of these tissues. Clinical signs of hypercalcaemia are non-specific, and are usually referable to the urinary system (polyuria / polydipsia), the gastrointestinal system (inappetance and vomiting), the nervous system (weakness, lethargy, depression, twitching / shaking and muscle wasting) and the cardiovascular system (arrhythmias). In particular, hypercalcaemia can lead to renal damage, which may ultimately result in a severe and irreversible nephropathy. Mild hypercalcaemia (serum calcium > 3.0 mmol/l) is often found in hypoadrenocorticism and primary renal failure, but more significant hypercalcaemia (serum calcium > 3.7 mmol/l) is seen with certain malignancies, particularly lymphosarcoma and anal gland adenocarcinoma, and in primary hyperparathyroidism. The differential diagnosis of hypercalcaemia is covered elsewhere (Weller *et al* 1985, Elliott *et al* 1991).

Hypocalcaemia

Calcium is essential for muscle contraction and it stabilises the neuromuscular cell membrane by decreasing its permeability to sodium. In hypocalcaemia this stabilising effect is lost and the neuromuscular cell becomes excessively irritable. Hypocalcaemic tetany occurs when the serum calcium falls below 2.2 mmol/l, which may result from post-parturient eclampsia, terminal renal failure, primary hypoparathyroidism, protein-losing enteropathy or severe alkalosis.

Hypermagnesaemia

Magnesium imbalances are not common in small animals. Hypermagnesaemia will interfere with calcium utilisation and cause signs similar to those of hypocalcaemia. Most reported cases are iatrogenic following administration of magnesium sulphate.

Hypomagnesaemia

Hypomagnesaemia is frequently accompanied by low serum calcium concentrations because of the ability of chronic hypomagnesaemia to inhibit the release of parathyroid hormone. Although rare, it should be considered as a cause of weakness, depression and ataxia in cases of intestinal malabsorption and renal disorders with high urine output.

ENDOCRINE DISORDERS

A number of endocrine disorders may be associated with episodic weakness and collapse. The most important in this respect are insulinoma, hypoadrenocorticism hypoparathyroidism and phaeochromocytoma. Hyperadrenocorticism (Cushing's disease), hypothyroidism and diabetic ketoacidosis or more rarely non-ketotic hyperosmolar diabetic syndrome may produce signs of weakness and / or collapse, but the history and other presenting signs are likely to suggest the diagnosis to the clinician.

Insulinoma

Insulin-secreting pancreatic islet cell tumours (insulinomas) commonly present as episodic weakness or syncope, related to hypoglycaemia. Seizures may also be the presenting sign. Most insulinomas in dogs are malignant, and metastasis to regional lymph nodes and the liver is common. Secretion of the beta cells causes hyperinsulinism and hypoglycaemia. Glucose is the principal source of energy for neurons, and as the brain cannot store significant amounts of glucose, a constant supply is required. Prolonged hypoglycaemia causes ischaemic neuronal cell damage identical to that caused by hypoxia.

Insulinomas usually occur in dogs over 5 years of age. There is no sex or breed predilection. Clinical signs are usually transient, lasting only a few minutes to an hour and occur days or even weeks apart. Episodes may include inco-ordination and ataxia, paraparesis, disorientation, apparent blindness and abnormal behaviour, and can progress to collapse and seizures. Peripheral neuropathy may also be seen, causing episodic weakness (Braund *et al* 1987, Schrauwen 1991).

Most animals have a persistently low blood glucose after fasting (<3.0 mmol/l) with a coexisting serum insulin concentration greater than 20 mU/l. Some patients

appear to adapt to the low glucose state by an unknown mechanism, and may appear clinically normal despite a blood glucose of 1.5 mmol/l. Hypoglycaemia should suppress insulin secretion, so concomitant hyperinsulinism is suggestive of an islet cell tumour. An insulin:glucose ratio greater than 4.2 U/mol is considered diagnostic (Dunn *et al* 1992). An intravenous glucose tolerance test, oral glucose tolerance test or glucagon tolerance test can be performed. These tests transiently increase blood glucose, but the peak blood glucose concentration is lower and returns to normal much faster than in normal animals. When an insulinoma is strongly suspected and the laboratory results are equivocal, exploratory laparotomy is indicated.

Surgical removal of the pancreatic mass and any involved lymph nodes can resolve the clinical signs for a year or more (Chrisman 1980, Dunn *et al* 1993).

Hypoadrenocorticism

Adrenocortical insufficiency has been associated with the following conditions: (a) primary idiopathic hypoadrenocorticism, (b) mitotane (o,p'DDD)-induced adrenocortical necrosis, (c) iatrogenic glucocorticoid-induced adrenocortical atrophy, (d) haemorrhage or infarction of the adrenal glands, (e) mycotic or neoplastic involvement, (f) surgical adrenalectomy, and (g) secondary hypoadrenocorticism due to pituitary insufficiency (Herrtage 1989). Primary idiopathic hypoadrenocorticism is due to atrophy of the adrenal cortex, probably as a result of immune-mediated destruction, and leads to deficiencies in both mineralocorticoid and glucocorticoid production.

Aldosterone is the major mineralocorticoid and deficiency results in sodium and chloride loss, and potassium and hydrogen retention. Hyponatraemia induces lethargy, depression, nausea, hypotension, impaired cardiac output, reduced renal perfusion, and hypovolaemic shock. Hyperkalaemia causes muscle weakness, hyporeflexia and impaired cardiac conduction. Glucocorticoid deficiency causes decreased tolerance of stress, loss of appetite and a normocytic, normochromic anaemia.

Other clinical signs include a chronic inability to gain weight, weight loss, periodic vomiting and / or diarrhoea, lethargy and weakness. Polydipsia and polyuria are also noted in some patients and occasionally severe gastrointestinal haemorrhage will occur, which may confuse the diagnosis (Medinger *et al* 1993). These signs may vary over a period of weeks or months then suddenly culminate in acute hypotensive collapse. Addisonian crises occur acutely with or without any associated stress trigger.

Bradyarrhythmias are common and the ECG is useful for detecting the various changes associated with hyperkalaemia. The most common abnormalities include flattened P waves, increased T wave amplitude, broadened QRS complexes and atrial standstill. The latter is associated with profound bradycardia.

The biochemical findings include hyperkalaemia and hyponatraemia (Na:K ratio <25:1; normal >27:1). Additional abnormalities include mild to moderate hypochloraemia, uraemia, hyperphosphataemia, and metabolic acidosis. Mild hypercalcaemia is often present, but hypoglycaemia is rarely seen. In rare cases, hypoadrenocorticism may be present with normal electrolytes. The definitive diagnosis is made by measuring serum cortisol concentrations before and after ACTH stimulation. Plasma cortisol concentrations are low and fail to respond to ACTH.

Treatment in an acute crisis includes correcting volume depletion with normal saline, correcting the electrolyte imbalance, replacing glucocorticoids and correcting life-threatening arrhythmias and acidosis. Maintenance therapy consists of mineralocorticoid replacement, salt supplementation and glucocorticoids given in times of stress.

Hypoparathyroidism

Primary hypoparathyroidism is an uncommon endocrine disorder characterised by decreased production and / or release of parathyroid hormone, which results in profound hypocalcaemia and mild to moderate hyperphosphataemia (Bruyette and Feldman 1988, Peterson *et al* 1991). The clinical signs are caused by the physiological effects of hypocalcaemia on the neuromuscular system. Clinical signs include seizures, focal trembling, generalised muscle fasciculations, ataxia, weakness, panting, and polydipsia and polyuria. Frequently, the neuromuscular signs are episodic and precipitated by exercise, excitement or stress.

The diagnosis is rarely difficult because resting hypocalcaemia (<2.2 mmol/l) is usually present even if the patient is clinically normal. Laboratories usually measure total serum calcium, although only the ionized fraction is physiologically active. Hypoalbuminaemia may result in a reduction in total serum calcium, but does so at the expense of protein-bound calcium rather than the ionized fraction. Thus albumin concentrations should be determined at the same time as calcium.

Phaeochromocytoma

Tumours of the adrenal medulla (phaeochromocytomas) are rare in dogs and have not been reported in cats (Herrtage 1989). Phaeochromocytomas are usually benign and may secrete excessive amounts of catecholamines.

Clinical signs may relate to an abdominal mass compressing adjacent structures or to the secretion of adrenaline and noradrenaline. Secretion of catecholamines may be intermittent or persistent and can cause hypotension or hypertension, tachycardia and tachyarrhythmias with associated weakness and trembling. Seizures, head pressing, epistaxis and retinal haemorrhages may also be noted. Intermittent

secretion of catecholamines is very likely to give rise to episodic weakness and collapse.

Surgical removal of the tumour is the treatment of choice.

Hyperadrenocorticism (Cushing's Disease)

Hyperadrenocorticism is associated with excessive production or administration of glucocorticoids and is one of the most commonly diagnosed endocrinopathies in the dog (Herrtage 1989). Feline hyperadrenocorticism is rare, but resembles the canine disorder in many respects.

Affected dogs usually develop a classic combination of clinical signs. These signs include polydipsia / polyuria, polyphagia, abdominal distension, muscle wasting and weakness, skin and hair coat changes and anoestrus or testicular atrophy. Muscle wasting and weakness may be profound in some cases, leading to episodic weakness and / or collapse associated with exercise. Muscle wasting occurs as a result of increased catabolic rate and inhibition of myofibrillar proteins. Type II muscle fibres are more sensitive to the effects of glucocorticoids than type I fibres (Shelton and Cardinet 1987). Occasionally dogs with hyperadrenocorticism develop myotonia (see above).

Fairly consistent haematological and biochemical changes are found on routine laboratory tests. These include lymphopenia, eosinopenia, neutrophilia, increased alkaline phosphatase, ALT and cholesterol, high normal blood glucose, and decreased blood urea. The diagnosis is confirmed by an ACTH stimulation test or a low-dose dexamethasone suppression test.

Treatment of hyperadrenocorticism is reviewed elsewhere (Herrtage 1989).

Hypothyroidism

Hypothyroidism is the most common endocrinopathy seen in the dog, and usually affects young to middle-aged dogs of the larger breeds. The clinical signs are very variable and often vague. Affected dogs may present with any one of a combination of the following clinical signs; lethargy, slow heart rate, poor exercise tolerance, obesity, intolerance to cold, alopecia, recurrent skin infections, and abnormal oestrus cycles or a lack of libido. Occasionally signs of neuromuscular dysfunction are seen and these include weakness, stiffness, decreased conscious proprioception and muscle wasting (Feldman and Nelson 1987). Peripheral neuropathies can result from mucinous deposits in and around the nerve fibres and may also affect the cranial nerves (Bichsel *et al* 1988). A myopathy associated with type II fibre atrophy has also been described (Braund *et al* 1981). Episodic weakness and collapse may be seen in those patients in which lethargy, poor exercise tolerance, obesity and muscle wasting are most marked.

Confirmation of the diagnosis can be difficult. Reduced thyroid hormone concentrations and a subnormal response to TSH are considered the most sensitive tests. Thyroid supplementation should resolve the clinical signs.

Hyperthyroidism

Hyperthyroidism results from excessive secretion of thyroid hormones and is one of the most common endocrine disorders in cats. It is a rare endocrinopathy in dogs.

The historical, clinical and laboratory features have been reviewed (Peterson *et al* 1983, Thoday and Mooney 1992). The most common clinical signs include weight loss despite an increased appetite, polyuria / polydipsia, tachycardia, hyperactivity, diarrhoea and vomiting. About 10% of cats with hyperthyroidism become depressed, lethargic and anorectic and are classified as apathetic. The diagnosis of hyperthyroidism is confirmed by elevated serum thyroxine concentrations.

Some cats with advanced hyperthyroidism may show marked muscle weakness. This may be manifest by ventroflexion of the neck, muscle tremors, gait disturbances (ataxia, incoordination and an inability to jump), muscle atrophy and collapse (Joseph and Peterson 1992). Plasma CK concentrations may be raised in some of these cats. This generalised weakness will tend to resolve when the hyperthyroidism is treated and the euthyroid state is re-established.

SUMMARY

Despite intensive investigation, a few cases of episodic weakness and collapse will defy diagnosis. It is more likely that a diagnosis will be made in these cases if the episode can be precipitated and reproduced. Repeating the physical examination, rectal temperature, routine haematology and biochemistry, blood gas analysis and ECG during or immediately after an episode, is likely to be helpful in these difficult cases and may suggest further avenues to be considered.

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CHAPTER FOURTEEN

Canine and Feline Peripheral Polyneuropathies

Ian D. Duncan

INTRODUCTION

The study of peripheral neuropathy in small animals is an expanding field in veterinary neurology. While dogs with epilepsy and intervertebral disc disease are still likely to be the most common neurological diseases that the small animal practitioner encounters, dogs and cats with polyneuropathy will be recognised with increasing frequency. This is more likely to be because of an increasing awareness of the signs seen in animals with neuropathy rather than an actual increase in the frequency of these disorders (Duncan & Griffiths 1984). The signs of paresis and ataxia, so commonly associated with the myelopathy of intervertebral disc herniation or other spinal cord diseases, are now also recognised as potentially being of peripheral nerve origin. In addition, peripheral nerves and the muscles they supply are much more accessible to both ancillary testing and biopsy than tissue in the central nervous system, thus increasing the likelihood of diagnosis. This chapter reviews the current state of knowledge on polyneuropathy in small animals, and provides the practitioner with a background to the range of these disorders and the means of diagnosing them.

The Peripheral Nervous System (PNS)

The PNS is defined as consisting of those parts of motor neurons, primary sensory neurons and autonomic neurons that lie outside the boundaries of the central nervous system. Although motor neurons originate in the spinal cord from ventral horn cells and the brain stem from cranial nerve nuclei, disorders of these structures are not classified as peripheral neuropathies. This may seem inconsistent, as disorders of ventral horn cells will result in LMN signs. However, their exclusion from the overall "neuropathy" classification is a useful separation from a nosological standpoint (Duncan 1987).

Clinical Examination and Signs of Polyneuropathy

A standard approach to the examination should be taken in any animal with neurological disease. After the history is taken, a complete physical examination is performed. A number of neuropathies are associated with a multisystemic disease, for example, diabetes mellitus and neoplasia, so the physical examination should not be omitted even though the dog is clearly paretic, or ataxic. This is then followed by the detailed neurological examination, which is described previously in this book (Chapters 2 & 3).

The first part is the evaluation of the animal's gait and muscle strength, which should be done on a non-slippery surface. The animal's strength should be evaluated even if it is reported by the owner to be paraplegic or tetraplegic, as it may only be severely weak or the weakness may be asymmetrical. If possible, the dog should be walked back and forth several times with the examiner viewing the animal from the back, front and side. It may be necessary to walk or run the dog up stairs to demonstrate weakness. With a cat, examination of the gait is performed in the examination room or on a carpeted area.

After evaluation of the gait, the second part of the examination, evaluating the postural reactions, is performed. These tests will only be summarised as they are described in detail elsewhere (deLahunta 1983; Oliver & Lorenz 1983 and Chapter 3). Proprioception is assessed by testing paw position sense, sway response and "reflex stepping". There may be some difficulty in distinguishing proprioceptive deficits from weakness, as the animal may be unable to replace the limb because of paresis, and not as a result of proprioceptive deficits. However, paw position sense may be retained in animals that are paretic, almost up to the point of paralysis. Wheelbarrowing, hopping, hemistand, hemiwalk and postural thrust are tests used to demonstrate weakness in an individual limb or asymmetrical weakness. Finally, visual and tactile placing reflexes are tested, which require vision and intact tactile sensory receptors respectively, and the ability to flex the limb.

The third part of the examination is the evaluation of spinal reflexes, muscle tone and muscle bulk. Reflexes are evaluated with the dog or cat relaxed in lateral recumbency. The patellar reflex is the most easily evaluated stretch reflex and should be graded:- O = absent; + = hyporeflexic; 2+ = normal; 3+ = hyperreflexic; 4+ = clonus). Thoracic limb reflexes (biceps, triceps and extensor carpi radialis) should be tested,

but can be difficult to elicit and interpret. A pedal reflex should be elicited in each limb and the strength of flexion noted. At the same time, presence or absence of a pain response should be noted. Muscle tone is evaluated in all limbs and muscle bulk checked (already examined during postural reaction testing).

The final part of the neurological examination is the cranial nervous system (Chapter 2). Both motor (V, V11 and X) and sensory deficits (V) to the head can be seen in neuropathies and so this should not be omitted.

Signs of Polyneuropathy

The most frequent presenting signs in animals with peripheral neuropathy are paresis, ataxia, muscle atrophy, hyporeflexia and hypotonia. In most instances, paresis is present from the onset of exercise and thus is not exercise related. Frequently the history includes a report that the animal has difficulty in rising on the pelvic limbs. There may be temporal progression of the weakness, with the development of tetraparesis and sometimes tetraplegia. In general, the pelvic limbs are affected before the thoracic limbs, probably because of the greater length of the nerves of the pelvic limbs. The length of the nerve is thought to explain why the recurrent laryngeal nerve is frequently clinically affected in neuropathy, resulting in alteration or loss of bark. On occasions, denervation of the skeletal muscle of the oesophagus can result in megaoesophagus. Ataxia is a sign often seen in neuropathy and results from involvement of large diameter proprioceptive fibres or their cell bodies in sensory ganglia. Hyporeflexia and hypotonia can also arise from lesions in sensory nerves or ganglia, and from disease of motor fibres. Finally, muscle atrophy is commonly

Table 14.1: Differentiation between neuropathy and myopathy

	Neuropathy	**Myopathy**
Paresis	Yes	Yes
Ataxia	Yes (proprioceptive deficit)	No
Nociception	Can be lost in sensory neuropathy	Normal
Voice	Often changed or lost	Normal
Muscle bulk	Atrophy (not in demyelinating disease)	Frequent - sometimes hypertrophy
Muscle tone	Usually reduced	May be mildly reduced
Reflexes	Reduced to absent	May be reduced
Muscle pain	None (may be some tenderness on palpation in Coonhound paralysis)	Variable in polymyositis
Distribution of lesion	Frequently pelvic limbs first and worst, especially distal	Usually generalised but remember masticatory muscle myositis
Autonomic dysfunction	May be involved	None
Muscle dimple	None	Present in myotonic states
EMG/NCV	EMG - denervation potentials NCV - reduced amplitude, slowed conduction	EMG - spontaneous activity myotonia NCV - normal
Serum enzymes	Normal	Creatine kinase may be elevated
Biopsy	Muscle - denervation, fibre type grouping Nerve - **may** show abnormalities	Muscle - often useful and diagnostic Nerve - normal

seen in neuropathies and indicates degeneration of motor nerve fibres. In most neuropathies, autonomic function and pain perception (nociception) remain intact, and this may be useful in differentiating them from other neurological disorders. However, certain neuropathies almost exclusively affect either autonomic or nociceptive function, i.e. feline dysautonomia (see later and Chapter 12), and inherited sensory neuropathy (see later).

Ancillary Aids

Routine serum chemistry profiles, special biochemical tests and complete blood counts are infrequently of assistance in the diagnosis of polyneuropathy. However, they are essential in the diagnosis of metabolic diseases in which neuropathy may occur secondarily e.g. diabetes mellitus (blood glucose); hypothyroidism (TSH response); hypoglycaemia resulting from an insulinoma (blood glucose, insulin:glucose ratio). In cats, a rare inherited neuropathy associated with hyperlipaemia may be confirmed by measuring fasting lipoprotein concentrations (Jones *et al* 1986). CSF evaluation is also rarely helpful, but it may demonstrate an albumino-cytological dissociation in dogs or cats with polyradiculoneuritis (Cummings et al 1982). In polyradiculoneuritis, a lumbar collection of CSF is required, as the lesions are predominantly in the lumbosacral area (Cummings *et al* 1982).

Electrophysiological tests are often the mainstay of the diagnostic workup in a dog or cat with polyneuropathy. These tests are detailed elsewhere in this book - Chapter 4.

Diagnosis of Neuropathy

It is rare that the diagnosis of a neuropathy can be made on clinical grounds alone, but in certain neuropathies a common antecedent event (e.g. in Coonhound paralysis) or a familial trait (e.g. giant axonal neuropathy) can be diagnostic pointers. More often, the diagnosis is made from the combined information derived from the clinical examination, electrophysiology, and muscle and nerve biopsy. Laboratory data may or may not implicate a metabolic cause, and the electrophysiology will help determine the underlying pathology, i.e. whether it is a demyelinating or axonal disease. The muscle and nerve biopsy will confirm this and may permit a diagnosis to be made. The application of such an approach to diagnosis will undoubtedly increase the diagnostic rate but, as in man where more sophisticated testing is the norm, many neuropathies will remain idiopathic in origin (Dyck *et al* 1984). Despite this cautionary note, such an approach has advanced the understanding and knowledge of small animal peripheral neuropathy greatly in the last decade and will continue to do so.

Differential Diagnosis

In most animals with paresis and ataxia, clinical examination will determine whether this is a result of disease of the CNS or neuromuscular system (PNS, neuromuscular junction and muscle). However, it is sometimes more difficult to differentiate a neuropathy from a myopathy or a disturbance of neuromuscular transmission on clinical grounds alone. In most cases this differentiation is made not on a single difference but on a combination of signs (Table 14.1). Differentiation of neuropathy from disorders of neuromuscular transmission is not usually difficult. Myasthenia gravis (MG), the most important of these, is usually associated with exercise intolerance and most patients have megaoesophagus (Duncan & Griffiths 1986), which is much less common in neuropathy. The response to anticholinergic drugs in MG is the final clue (Chapter 13).

Response of the Peripheral Nerve to Disease

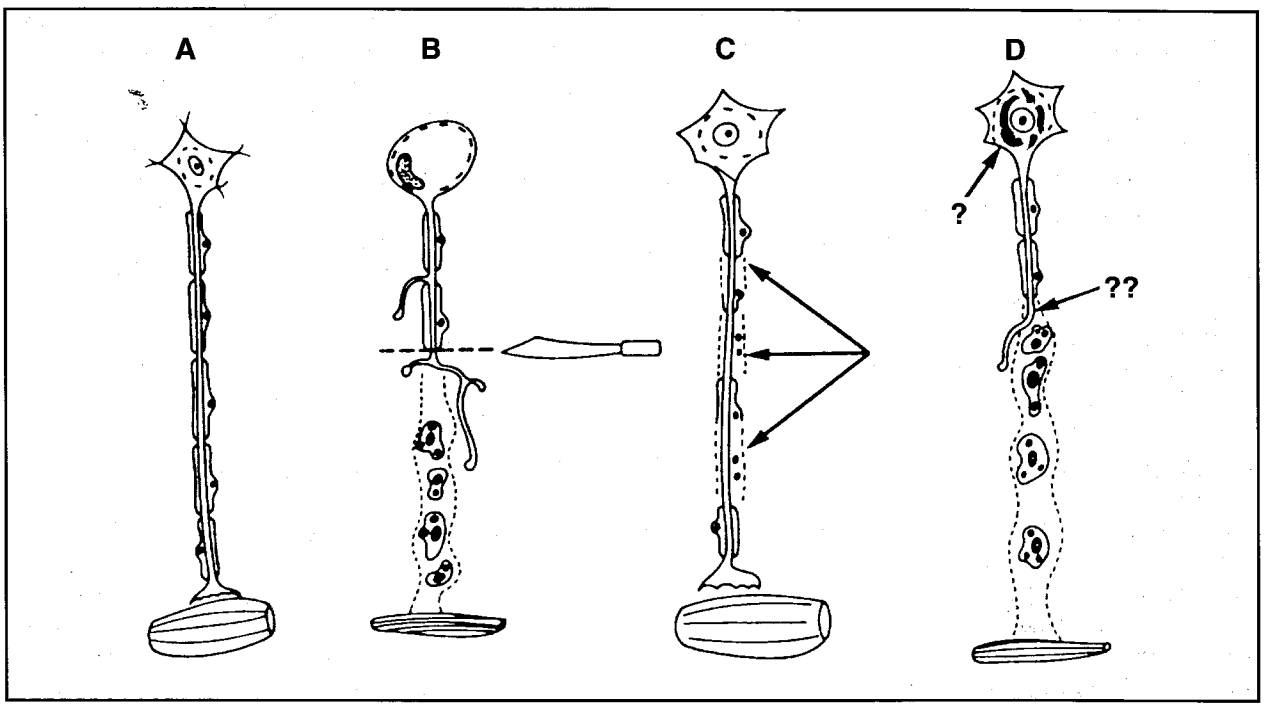
Peripheral nerves consist of large, medium and small myelinated nerve fibres and non-myelinated fibres, randomly mixed in groups known as fascicles, which are surrounded by the perineurial connective tissue sheath. These structures have a very stereotyped response to injury (Figure 14.1).

Transection of a nerve results in degeneration of all the fibres distal to the section (Wallerian degeneration).

Distal degeneration of nerve fibres can also occur in non traumatic situations; e.g. neurotoxic poisoning or certain familial neuropathies. Often this primarily affects long, large diameter myelinated nerve fibres and such a process is known as the dying back phenomenon, or distal axonopathy (Dyck *et al* 1984). As this process initially affects long, large diameter nerve fibres, clinical evidence of neuropathy is first seen in the distal muscles of the pelvic limbs e.g. gastrocnemius and cranial tibial muscles.

Demyelination is a random process in comparison and results in focal (paranodal or segmental) loss of the myelin sheath but leaves the axon intact. As a result, muscle fibres do not become denervated and no neurogenic atrophy is seen in the muscle biopsy, unlike in neuropathies where there is axonal degeneration with accompanying neurogenic muscle atrophy.

Repair of the nerve following both axonal degeneration and demyelination is possible, although faster and more complete in the latter; this is reflected in the faster clinical recovery seen following demyelination. Successful re-innervation of muscle following the transection of a nerve will depend upon the distance between the muscle and the site of nerve trauma, the apposition of the cut ends of the nerve, and the presence or absence of neuroma formation.



14.1: The basic disease processes affecting the peripheral nerves are detailed in this diagram.
A. Normal.
B. Wallerian degeneration causes central chromatolysis of the nerve cell body as well as distal degeneration of the axon.
C. Segmental demyelination of individual myelin sheaths or Schwann cells causes patchy damage.
D. In axonal neuropathy, the disease may affect either the cell body or the peripheral axon, causing axonal breakdown. In both forms of axonal degeneration, the muscle becomes atrophied.
(From Bradley, W. G.: Disorders of Peripheral Nerves. Oxford. Blackwell Scientific Publications, 1974, with permission.)

The further from the muscle and the larger the gap between the cut ends, the less the chances of recovery. Axonal regeneration in non-traumatic neuropathies also often occurs but may be abortive because of ongoing axonal disease. Careful evaluation of the nerve biopsy (LM and EM, and single teased nerve fibres) will allow a pathological classification of the disease to be made, i.e., whether it is a predominantly axonal or demyelinating neuropathy or a mixture of both (Braund 1994). Most often neuropathies are "mixed", with pathological evidence of both degeneration and demyelination.

Classification of Neuropathies

There are a number of different ways of classifying neuropathies (Duncan 1987) and these are summarised below.

Anatomical

Polyneuropathy is the term used for disease of multiple peripheral nerves. Many neuropathies symmetrically affect the distal parts of long, large diameter myelinated nerve fibres (distal axonopathy - see above), and so the distal limb muscles in the pelvic limbs are affected first and most severely. Occasionally the opposite can occur; i.e. proximal limb muscles first, but this is rare.

Mononeuropathy is the term for spontaneous neuropathy clinically affecting only one nerve. If a number of nerves are affected randomly, the term "mononeuropathy multiplex" is used.

Polyradiculoneuropathy is the term used if the site of the lesion is in the nerve roots.

Pathological

- Axonal degeneration
- Demyelination
- Sensory Neuronopathies

Aetiological

The following list contains the known causes of peripheral neuropathy in animals:

Genetic, Inflammatory, Traumatic, Immune-mediated, Metabolic, Neoplastic, Infectious, Ischaemic, Toxic.

Clearly all causes of disease in general can affect the PNS. The final classification of a neuropathy usually includes all of the above types of classification e.g. the dog has a distal axonopathy with both axonal degeneration and demyelination caused by an autosomal recessive trait.

NEUROPATHIES

The following discussion briefly outlines the peripheral neuropathies seen in the dog and cat (Table 14.2). This discussion will emphasise those of most importance in the United Kingdom and will briefly describe those seen in North America. More details of these can be found elsewhere (Duncan & Griffiths 1984; Griffiths & Duncan 1986; Duncan & Griffiths 1986).

Inherited Canine Neuropathies

Sensory neuropathy in Dachshunds

Aetiology and pathogenesis. This disease appears likely to be inherited as an autosomal recessive trait. It has only been described to date in the United Kingdom (Duncan & Griffiths 1982). Sensory nerve biopsy demonstrates a severe loss of myelinated fibres with diffuse unmyelinated fibre abnormalities (Duncan, Griffiths & Munz 1982). A case report in a Border collie described many similar clinical and pathological abnormalities to the Dachshunds (Wheeler 1987).

Clinical findings. Affected dogs are usually noted to have a pelvic limb ataxia from the time they start to walk. There is no paresis. Proprioception is slow to absent, as are placing reflexes. Nociception is decreased or absent over the whole body, and there may be rare evidence of self-mutilation. There may be autonomic involvement as the dogs may dribble urine and have a history of unexplained bouts of vomiting. Motor nerve conduction studies and EMG are normal, but sensory nerve conduction is often abnormal. Confirmation of the diagnosis is made on biopsy of a sensory nerve.

Treatment. None, but affected dogs can usually survive quite normally without therapy.

Sensory neuropathy in Pointers

Aetiology and pathogenesis. This neuropathy is inherited as an autosomal recessive disease. It is found in Short-haired pointers in Europe, and English pointers in the United States. The underlying lesion is a developmental disorder of primary sensory neurons, with only minimal evidence of degeneration of these cells (Cummings, deLahunta & Winn 1981).

Clinical findings. The first signs of neuropathy are usually seen under six months of age, when mutilation of the extremities is found. In the pelvic limbs there is complete anaesthesia of the digits. This is also reduced

Table 14.2: Known canine and feline polyneuropathies

INHERITED	ACQUIRED
CANINE	
Sensory neuropathy - Dachshunds (autosomal recessive)*	Distal denervating disease
Sensory neuropathy - Pointers (autosomal recessive)*	CHP/polyradiculoneuritis
Giant axonal neuropathy - GSDs (autosomal recessive)*	Sensory neuropathy
Progressive axonopathy - Boxer dogs (autosomal recessive)*	Toxoplasma - polyradiculoneuritis
Hypertrophic neuropathy - Tibetan mastiffs (autosomal recessive)*	Brachial plexopathies Endocrine neuropathies
Globoid cell leukodystrophy (autosomal recessive)*	Trauma Paraneoplastic Neoplasia Individual case resports (usually idiopathic)
FELINE	
Neuropathy of inherited hyperchylomicronaemia Niemann Pick disease*	Ischaemia Diabetes mellitus Feline dysautonomia Trauma Neoplasia Individual case reports
*Putative inherited trait	

in the thoracic limbs and trunk. By comparison, other sensory modalities, in particular proprioception, are intact, and the stretch reflexes are normal.

Treatment and prognosis. There is no known treatment and self-mutilation will lead to considerable destruction of distal limb tissue.

Giant axonal neuropathy (GAN)

Aetiology and pathogenesis. This is inherited as an autosomal recessive trait in German shepherd dogs, although only one family of these dogs has been described in the United Kingdom (Duncan & Griffiths 1979; Duncan & Griffiths 1981; Duncan *et al* 1981). GAN is a classical distal axonopathy, with lesions being found first in distal nerves in the pelvic limbs and at the end of long tracts in the CNS (Duncan & Griffiths 1979). In both PNS and CNS, axons of both myelinated and unmyelinated fibres are focally distended with abnormally accumulated neurofilaments. These swellings finally result in degeneration of the distal axon.

Clinical findings. The first signs are seen between 12-15 months of age when pelvic limb ataxia is noted. This progresses, with development of distal muscle weakness and atrophy, proprioceptive deficits, hypotonia and hyporeflexia. Pain sensation is reduced because of the involvement of small axons, and megaoesophagus always develops. By 18-24 months the dogs may be extremely weak in the rear with some thoracic limb weakness. EMG is useful in the initial demonstration of the distal nature of the denervation in the pelvic limbs. Diagnosis is made on pathognomic nerve biopsy changes found in a motor or sensory nerve.

Treatment and prognosis. None; poor outlook as megaoesophagus frequently leads to aspiration pneumonia.

Progressive axonopathy of Boxer dogs

Aetiology and pathogenesis. This disease is inherited as an autosomal recessive trait. To date, it has only been described in certain breeding lines in the United Kingdom (Griffiths 1980; Griffiths 1986). Its early onset suggests that changes may be present at birth or begin in utero. Axonal swellings within the nerve roots of the lumbar cord, with resultant axonal atrophy in more distal portions of the nerves, are the hallmark of this neuropathy. The myelin sheath changes which occur are thought to be secondary to the underlying axonal pathology (Griffiths *et al* 1987). Similar axonal changes are seen in the CNS.

Clinical findings. The first signs are seen after 2-3 months of age but may be preceded by patellar areflexia at one month. The pelvic limbs show a marked ataxia with proprioceptive deficits, hypotonia and hyporeflexia, but no muscle atrophy. The thoracic limbs may be involved late in the disease and there may be fine ocular tremor and head bobbing. The signs may not worsen after initial progression over the first two years of life. The diagnosis is made on a clinical and breed basis and is usually straightforward. Additional tests could include sensory nerve electrophysiology, which is abnormal, and a sensory nerve biopsy.

Treatment and prognosis. There is no treatment, but affected animals may live comfortably for considerable periods of time.

Canine hypertrophic neuropathy

Aetiology and pathogenesis. This neuropathy, which is found in the Tibetan mastiff in the USA, is inherited as an autosomal recessive trait (Cummings *et al* 1981; Cooper *et al* 1984). It is predominantly a demyelinating neuropathy unlike most other inherited canine neuropathies. Myelin sheath changes, associated with the accumulation of filaments in the cytoplasm of Schwann cells, occur early in life resulting in demyelination and remyelination. Subsequently, there is little further active demyelination and so, histologically, there is rare evidence of hypertrophic changes (i.e. onion bulbs).

Clinical findings. The first signs are seen at about six weeks of age when paresis of the pelvic limbs and then the thoracic limbs (eight weeks) occurs. Hypotonia and hyporeflexia are seen but proprioception is intact. The weakness progresses with muscle atrophy developing and the adoption of a plantigrade stance. The voice may change as a result of involvement of the recurrent laryngeal nerve. These signs may not worsen and indeed, some strength may be regained if dogs are maintained on wood shavings and a smooth floor (Cooper *et al* 1984).

Treatment and prognosis. Apart from management changes during the early post-natal period there is no therapy but improvement, although not full recovery, can be seen.

Acquired Canine Neuropathies

Distal denervating disease

Aetiology and pathogenesis. This disease appears to be limited to the United Kingdom where it is one of the most common canine neuropathies (Griffiths & Duncan 1979a). The lesion is restricted to the intramuscular nerves or terminal motor branches of long motor nerves, where degeneration is found. Any age, breed or sex of dog can develop this disease and there are no known common epidemiological features.

Clinical findings. Affected dogs present with a history of progressive weakness involving all four limbs occurring over a few days to weeks, which often progresses to tetraplegia with cervical weakness and loss of bark. Reflexes are absent and there is marked hypotonia. Proprioception is present up until the stage that the dog is too weak to stand, and pain perception is retained. With time, marked appendicular muscle atrophy develops. EMG examination reveals diffuse evidence of denervation in practically all skeletal muscles with abnormal motor nerve conduction studies. The diagnosis is made by the exclusion of other possible causes. Nerve biopsy is usually unhelpful as the lesion is distal to the point at which biopsies are taken.

Treatment and prognosis. In practically all dogs with this disease, the outlook is excellent. As spontaneous recovery occurs, treatment consists of careful nursing care to prevent decubital ulcers, and hand feeding usually with soft food or gruel. Recovery should be seen within a 4-6 week period. Relapses have not been documented to date.

Polyradiculoneuritis - Coonhound paralysis (CHP)

Aetiology and pathogenesis. A polyradiculoneuritis seen in dogs that have had a previous racoon bite is the most common peripheral neuropathy in North America (Cummings & Haas 1967; Cummings *et al* 1982). Although racoons are not present in Europe, occasional cases of polyradiculoneuritis have been reported. Similarly, cases of polyradiculoneuritis in some dogs in North America and in Europe that have not been bitten by a racoon have also been documented (Northington & Brown 1982; Griffiths *et al* 1983). The actual relationship between the antecedent event in CHP, i.e. the racoon bite and the development of the nerve root lesion, is not clear. The disease has been transferred by the injection of racoon saliva into a dog that previously had bouts of CHP, but this has proved difficult to repeat (Holmes *et al* 1979) There may be a delayed hypersensitivity reaction against myelin caused by a protein constituent of racoon saliva. Although the antecedent events in the racoon and non-racoon associated polyradiculoneuritis may be different, the end stage is similar, with nerve root inflammation, demyelination and axonal degeneration.

Clinical findings. In CHP, dogs that have been bitten by a racoon 10-14 days previously develop a weakness in the pelvic limbs, initially apparent by the development of a stilted gait. The weakness progresses to tetraparesis and often tetraplegia with a loss of bark. Likewise, the cervical muscles may also be weak with an inability to raise the head. Pedal reflexes are lost but the dog may be hyperaesthetic. An EMG examination shows diffuse evidence of denervation as in distal denervating disease. Nerve conduction studies may show some slowing of nerve conduction velocity and eventual failure of conduction (Cummings *et al* 1982).

Treatment and prognosis. Treatment consists of careful nursing but no specific medical therapy. These dogs can eat and drink if assisted and have never been reported to develop a megaoesophagus. Their outlook is excellent and recovery should take between 4-8 weeks, depending on the initial severity of the neuropathy. Occasionally, the severe involvement of intercostal muscles can lead to respiratory difficulties and sometimes death. The dog should be placed on a respirator if necessary.

Sensory neuronopathy

Aetiology and pathogenesis. There have been several recent reports of series and individual case reports of dogs with ataxia and sensory disturbance over the face and body that are of considerable interest (Carmichael & Griffiths 1981; Cummings, deLahunta & Mitchell 1983; Wouda *et al* 1983; Steiss *et al,* 1987). In all of these dogs (except the first mentioned where only the sensory branches of cranial nerve V were involved), there was evidence of a loss of sensory neurons in the spinal ganglia, with resultant loss of fibres in sensory nerves and in the sensory tracts of the spinal cord. This neuronal cell loss frequently was associated with collections of mononuclear cells with occasional degenerating neurons being noted. In all of these dogs the aetiology was unknown, but comparisons were made with similar human conditions, and to neurotoxic poisons such as adriamycin, which preferentially can cause sensory neuronal death.

Clinical signs, In the majority of these dogs, the ataxia seen was associated with conscious proprioceptive deficits. There was evidence of hyporeflexia and hypotonia but no muscle atrophy, except of the masticatory muscles in some dogs (Cummings *et al* 1983). Pain sensation was usually reduced or absent in the territory involved, i.e. over face or limbs. Megaoesophagus was seen in a few dogs. In the case of Carmichael and Griffiths (1981) there was a sensory loss only over the head (trigeminal nerve - maxillary and ophthalmic branches) with no involvement of the mandibular nerve (motor branch) and absence of a sensory ataxia.

Treatment. There is no known therapy as the cause of these sensory neuronopathies is unknown. The course is likely to be progressive.

Protozoal polyradiculoneuritis

Aetiology and pathogenesis. In utero infection of a pregnant bitch with a protozoan parasite, which recent work indicates is *Neospora caninum* (Dubey *et al*

1988) and not *Toxoplasma gondii* as previously thought, can cause a severe polyradiculoneuritis and polymyositis in pups. The first clinical signs are seen between 4-8 weeks of age when paresis and pelvic limb ataxia are noted. This progresses to paraplegia with extreme rigidity of the pelvic limbs and the development of muscle atrophy. Pain sensation is intact. The inflammatory nerve root lesion is extremely severe with a widespread loss of nerve fibres (Jackson and Duncan, unpublished observations). As such, these lesions are not responsive to the standard medical therapy used in dogs with systemic protozoal infections and myositis. The outlook therefore is poor.

Brachial plexopathies

Occasionally dogs will develop subacute or chronic thoracic limb weakness and muscle atrophy (EMG shows denervation) without evidence of previous trauma (Duncan & Griffiths 1986). These are usually idiopathic in nature, although one report suggests an anaphylactic reaction associated with a horse meat diet as the cause. In that dog, microscopic studies of the brachial plexus showed a severe neuritis. In some dogs with brachial plexopathies, the pelvic limbs may eventually become involved and so these cases should be regarded as generalised polyneuropathies. In those that remain restricted to the brachial plexus, this may indicate an inflammatory neuropathy and so steroids treatment may be tried. A more distal nerve biopsy usually only shows evidence of axonal degeneration and so is not diagnostic.

Endocrine neuropathies

Hypoglycaemia. A recent report suggests that dogs with insulinomas can have subclinical microscopic evidence of neuropathy (Braund, Steiss, Amling *et al* 1987). This report followed anecdotal reports of clinical neuropathy in dogs with hypoglycaemia and insulinoma. We have seen one dog with insulinoma, which had an acute onset of neuropathy with paresis, hypotonia, hyporeflexia and pathological evidence of an axonal neuropathy (Duncan, Panciera and Cuddon - unpublished data). However, most dogs with insulinomas do not have clinical evidence of neuropathy, but the PNS should be carefully evaluated.

Diabetes mellitus. Neuropathy in diabetic dogs may occur but it appears to be less common than that seen in cats (see later).

Hypothyroidism. A neuropathy associated with serological evidence of hypothyroidism has been reported, mainly in large-breed dogs. Other systemic signs of hypothyroidism may also be seen (Braund 1994).

Traumatic neuropathy

Avulsion of the nerve roots forming the brachial plexus, as a result of the road traffic accident, is the most common traumatic neuropathy in the dog and cat. This, and sciatic nerve lesions, caused by trauma, are discussed elsewhere in this book (see Chapter 11).

Paraneoplastic neuropathy

There have been case reports in the veterinary literature suggesting that there could be an association between a neoplasm and neuropathy. The connection between neoplasia (often a lung tumour) and neuropathy in man is well recognised and also with various non-neural neoplasms. A connection between various non-neural neoplasms and subclinical neuropathy in a large series of dogs (as seen on histological evaluation of the ulnar and peroneal nerves), has been proposed (Braund, McGuire, Amling & Henderson 1987). The pathogenesis of the "distant" effect of such a tumour is still unknown, although there may be shared antigens between the tumour and nerve. A definitive association between clinical neuropathy and neoplasia in veterinary medicine has still to be made.

Peripheral nerve tumours

These can occur and most often affect the brachial plexus and its roots (See Chapter 11).

Individual case reports

There are numerous single case reports of idiopathic neuropathy in small animals in the veterinary literature, predominantly in the dog. These have been reviewed elsewhere (Duncan & Griffiths 1984).

Inherited Feline Neuropathies

Neuropathy of inherited hyperchylomicronaemia

Aetiology and pathogenesis. This recently described neuropathy in cats in New Zealand appears likely to be inherited as an autosomal recessive trait (Jones *et al* 1986). Affected cats were found to have resting hyperlipaemia, lipaemia retinalis and peripheral neuropathy (9 out of 20 with hyperlipaemia had neuropathy). The neuropathy was thought to result from compression of nerve trunks by the lipid granulomata (xanthomata) that develop. This compression affected peripheral nerves in a patchy fashion with notable axonal degeneration in either limb nerves, cranial nerves or the cervical sympathetic trunk.

Clinical findings. The first signs seen were usually paralysis of an individual limb. The term mononeuropathy multiplex could be applied to this neuropathy, as individual cats had involvement of the facial, tibial, peroneal, femoral, radial, trigeminal, or recurrent laryngeal nerves. In three cats, more than one nerve was involved. In addition, three cats developed a Horner's syndrome as a result of involvement of the cervical sympathetic trunk.

Treatment and prognosis. Resolution of the neuropathy, associated with a lowering of the lipaemia, occurred in three cats that were placed on a low fat diet.

Neuropathy of Niemann Pick disease

Aetiology and pathogenesis. The neuropathy was found in this lysosomal storage disease and has now been seen in three cats, two of whom were related (Cuddon *et al* 1989). It may be inherited in an autosomal recessive fashion. There is deficiency in the enzyme sphingomyelinase, which results in accumulation of sphingomyelin in neurons in the spinal cord and spinal ganglia, Schwann cells and in many cells (primarily associated with the mononuclear phagocyte system) in the viscera. In the PNS there is evidence of severe myelin breakdown and hypomyelination in the nerve roots.

Clinical sign. In the three cats, there was some variation in the signs seen. In one cat, limb and trunk tremor with a "stringhalt" like pelvic limb gait was noted from 4-6 weeks of age. This worsened over a 9-month period during which paraparesis, loss of tone and reflexes, and muscle atrophy developed. The other two cats presented at 5-7 months of age with progressive tetraparesis, hyporeflexia and hypotonia. Diagnosis during life can be made on enzyme quantitation of a liver biopsy or skin fibroblast cultures. A bone marrow biopsy can also be of use if foamy inclusions are seen in white blood cells.

Treatment and prognosis. This is a progressive, debilitating disease and there is no treatment. Cats with tremor alone can live normally for a number of months.

Acquired Feline Neuropathies

Ischaemic neuromyopathy due to thromboembolism

Aetiology and pathogenesis. This is a fairly common sequelae of cardiomyopathy in which thrombus development results from the formation of emboli which occlude one or more branches of the aorta (Flanders 1986). In particular, occlusion of the aortic trifurcation results in ischaemia to nerves and muscles in the pelvic limb, and occlusion of the brachial artery can also occur with thoracic limb paralysis. It is not the loss of blood supply *per se* that results in muscle and nerve ischaemia, but the release of sertonin (5HT) from platelets. In severe lesions there is ischaemia and degeneration of both muscle and nerve, but demyelination proximal to the areas of degeneration in nerve is also seen (Griffiths & Duncan 1979b). Regeneration of nerve can occur with re-establishment of blood supply (See Chapter 15).

Clinical findings. Following embolism of the aorta at its trifurcation, affected cats acutely develop paresis or paraplegia (depending on the degree of arterial block). Other signs include pain, loss of femoral pulses, cold limbs and pale foot pads and nails.

Treatment. This is aimed at treating the underlying cardiac disease, supplying analgesics if required, and aspirin therapy to inhibit platelet function (low dose - 25 mg/kg, per os) every third day for the rest of the cat's life (Flanders 1986). The prognosis depends on the initial severity of the ischaemia, the development of gangrene and the stage of the underlying cardiac disease. In all patients a guarded prognosis should be given, as although recovery from the neuropathy can occur, further bouts are likely as the underlying heart disease is not curable.

Diabetic neuropathy

Aetiology and pathogenesis. Polyneuropathy has now been clearly demonstrated in a number of cats with diabetes mellitus (Kramek *et al* 1984). Like human diabetic neuropathy, the exact causal relationship between the diabetes and the development of neuropathy is not known. In the cat the lesion appears to result in the distal degeneration of axons (distal axonopathy).

Clinical findings. The neuropathy in these cats presents as pelvic limb paresis, affected cats often adopting a plantigrade stance. There can be noticeable distal muscle atrophy and hyporeflexia. EMG examination shows evidence of denervation and nerve conduction velocity may be slowed. A nerve biopsy of a distal pelvic limb nerve shows evidence of axonal loss and myelin sheath changes.

Treatment and prognosis. Control of the diabetes, either in the newly diagnosed diabetic cat, or improved control in a cat already receiving insulin can reverse the signs of neuropathy. Severe, chronic neuropathy is less likely to respond to better diabetes control, however. Some cats will recover spontaneously from their diabetic state with subsequent partial to full clinical resolution of the accompanying polyneuropathy.

Feline dysautonomia

This has been an important feline neuropathy in the United Kingdom. It is the only small animal neuropathy known so far that almost solely affected the autonomic nervous system. It is the subject of another chapter in this text (see Chapter 12).

CHAPTER FIFTEEN

Special Neurology of the Cat

Andrew L. Hopkins

INTRODUCTION

In this chapter a problem-based approach to evaluating cats with neurological disease is adopted. The principles of lesion localisation described in Chapters 1- 3 apply to the cat, but it is important to realise that the disease processes seen in cats differ somewhat from those in dogs. A table of differential diagnoses for the major problems is presented for each neurological syndrome, with discussion of the more important diseases. Differential diagnoses are subdivided into the main disease processes affecting the nervous system, and are given using the 'DAMNIT - V" mnemonic discussed in Chapter 1.

The problems in feline neurology are considered under the following headings:

- Seizures, Altered Mentation and Behaviour Change
- Cranial Nerve Disorders
- Blindness
- Ataxia of the Head and Limbs
- Paraparesis, Paraplegia
- Tetraparesis, Tetraplegia
- Monoparesis, Monoplegia
- Micturition Disorders
- Self-Mutilation Syndromes

Seizures, Altered Mentation and Behaviour Change (Table 15.1)

Recognition of clinical signs such as seizures, behavioural changes (e.g. aggression, timidity), circling, head pressing and aimless wandering, allows localisation of the disease process to the forebrain (Figure 15.1). Visual deficits, proprioceptive deficits and abnormal mentation may also be seen.

Metabolic diseases, e.g. hepatic encephalopathy, tend to result in symmetrical and sometimes episodic

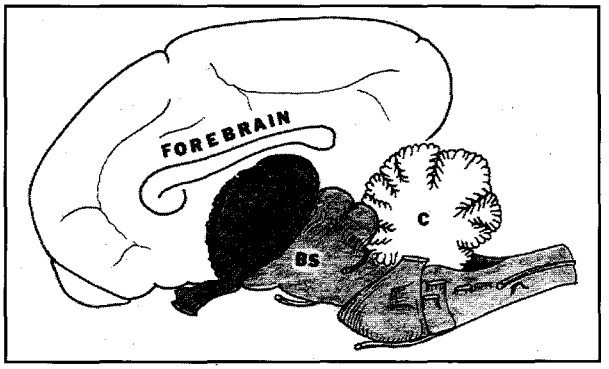


Figure 15.1: *Diagram of the brain illustrating the location of lesions causing:*
*Seizures, behaviour and mentation changes (**forebrain**),*
*Cranial nerve deficits and mentation changes (**brainstem - BS**)*
*Ataxia of the head and limbs (**cerebellum - C**).*

Table 15.1: *Differential diagnosis of seizures, altered mentation and behavioural change.*

Degenerative	Lysosomal storage disease
Anomalous	Hydrocephalus, hydranencephaly
Metabolic	Hepatic encephalopathy, Hypoglycaemia, hypoxia Hypocalcaemia, Hypernatraemia, Azotaemia
Nutritional	Thiamine deficiency
Neoplastic	Meningioma, Astrocytoma, ependymoma etc.
Inflammatory	FIP, Toxoplasma, FeLV, FIV, Cryptococcus, Parasites, Bacteria, meningoencephalomyelitis Feline spongiform encephalopathy
Idiopathic	
Toxic	OP, OC, Bromethalin, Metaldehyde, Lead
Traumatic	Bite, Malicious, RTA
Vascular	Cerebral ischaemic encephalopathy, Hypertension

neurological deficits. They may be excluded or confirmed by evaluation of serum biochemical parameters. If these are normal and intoxication is not suspected, cerebrospinal fluid (CSF) analysis and brain scan are indicated. Persistent or lateralising neurological deficits suggest structural intracranial disease.

While a cause for neurological disease should always be sought, occasionally, even after extensive diagnostic evaluation, the aetiology is not apparent. The term idiopathic is then sometimes applied. This appears particularly true of seizures, where the term idiopathic epilepsy is used. In dogs this term is sometimes used synonomously with inherited epilepsy. Although some cats may fit the same criteria, a genetic susceptibility to seizures has not been recognised in cats.

Degenerative diseases

Lysosomal storage diseases are rare, inherited, cellular metabolic disorders of which several are now recognised in cats, for example, alpha-mannosidosis in Persian cats, sphingomyelinosis in Siamese cats, and gangliosidosis in Korat cats (Evans 1989). A specific enzyme deficiency results in accumulation of cellular metabolic products, which disrupt normal cellular functions. While many organs may be affected, central nervous system (CNS) dysfunction is often first to become apparent. Signs are progressive and typically indicate diffuse cerebral and cerebellar dysfunction. Hepatosplenomegaly, skeletal abnormalities and ocular changes may also be encountered. Young cats (less than six months of age) are typically affected. The traits are inherited in an autosomal recessive fashion.

Anomalous

Infection with the feline infectious peritonitis (FIP) and panleucopaenia (FPL) viruses have been associated with the development of hydrocephalus or hydranencephaly in the neonate (Greene *et al* 1982; Krum *et al* 1975).

The teratogenic effects of griseofulvin are well recognised and include a variety of foetal abnormalities e.g. hydrocephalus, exencephaly and cyclopean deformities.

Metabolic diseases

Hepatic encephalopathy may be a sequel to acquired or congenital liver disease. Single, extrahepatic portosystemic shunts are the most common cause in cats (Center *et al* 1986). Clinical signs are usually episodic and include seizures, behavioural change, depression, and excessive salivation (ptyalism). Biochemical abnormalities include hypoalbuminaemia and low blood urea. Liver enzyme concentrations are variably affected and may be normal. Fasting and two hour post-prandial serum bile acid concentrations are usually abnormal. Definitive diagnosis may be substantiated by combinations of ultrasonography, nuclear scintigraphy, contrast portal venography and laparotomy. Diffuse hepatic disease or multiple shunts are usually managed medically. Medical therapy is aimed at reducing circulating toxins, which accumulate as a result of the hepatic insufficiency. Although commonly incriminated, serum ammonia concentrations do not necessarily correspond with the degree of encephalopathy. A diet with low protein (with a high biological value), low fat and high carbohydrate content is recommended (e.g. Hill's k/d[1]). Oral neomycin (20 mg/kg PO QID) and lactulose (0.25 - 1 ml PO SID - TID) are often used in combination to reduce the population of bacteria in the large intestine. Metronidazole has also been used in this context (Tams 1985). Long term prognosis with medical management of portosystemic shunts is poor, and surgical treatment is an option.

Azotaemia in advanced renal failure may be associated with profound depression, seizures (uraemic fits) and coma, but this is often a pre-terminal stage.

Neoplasia

Meningioma is the commonest intracranial neoplasm of cats. The majority are found rostral to the tentorium cerebelli and produce signs of forebrain disease. Most affected cats are males older than 10 years. Tumour growth is very slow and large sizes may be achieved before clinical signs develop. Multiple meningiomas have been reported. Diagnosis is based on the history, clinical signs, and computed tomography (CT) scanning or magnetic resonance imaging (MRI) (Figure 15.2). Areas of mineralization within the tumour may occasionally be seen on survey radiographs. Corticosteroid therapy may produce temporary improvement of clinical signs, but the long-term prognosis is poor without aggressive therapy. Surgical removal offers a good prognosis (Nafe 1979; Lawson *et al* 1984; Gallagher *et al* 1993).

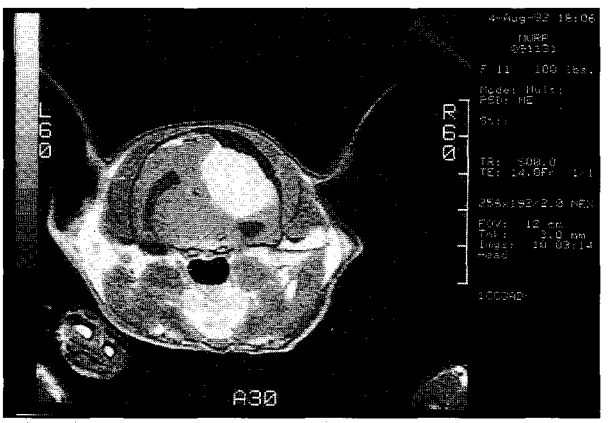


Figure 15.2: *Transverse magnetic resonance image of the brain at the level of the ears. A large contrast enhancing mass, typical of a meningioma, is seen in the right parietal cortex. There is hyperostosis of the overlying calvarial bone.*

Other neoplasms affecting the brain include ependymoma, pituitary adenoma, astrocytoma and lymphoma. Pituitary tumours may give rise to endocrine disturbances such as hyperadrenocorticism and diabetes mellitus, through over-secretion of adrenocorticotropic hormone and / or growth hormone (Lichtensteiger 1986).

Inflammatory disease

Feline infectious peritonitis. Infection with FIP virus may produce a wide range of neurological signs, and should be considered as a differential diagnosis in nearly all feline neurological disorders. Neurological signs are most commonly associated with the "dry" or non-effusive form of FIP. Single or multiple foci of pyogranulomatous inflammation may involve any part of the CNS (Kornegay 1978). Clinical signs are diverse and usually progressive, frequently including seizures, nystagmus and pelvic limb paresis. Pyrexia, depression and weight loss may also be apparent. Affected animals are typically under three years of age. Neurological disease associated with FIP virus infection is often accompanied by ocular disease such as anterior uveitis or retinal vasculitis. Diagnostic features of FIP virus infection include serum hypergammaglobulinaemia, and elevated CSF protein concentrations and white cell count (neutrophils and mononuclear cells). Serology is non diagnostic because of the high incidence of false positive and false negative results. Definitive diagnosis is made by histopathology. The prognosis is poor but temporary improvements may be achieved with corticosteroid therapy.

Toxoplasma gondii. Although the cat is the definitive host for *Toxoplasma gondii*, signs of systemic infection are uncommon. Affected cats usually show signs of pneumonia, but intracranial or spinal cord involvement may be seen (Dubey and Carpenter 1993). Neurological signs are usually progressive. They often include seizures, behavioural changes and paraparesis. CSF analysis may reveal elevations in the white cell count and protein concentration. Neurological signs may also be accompanied by clinical and biochemical evidence of other organ involvement, for example, uveitis, chorioretinitis, pneumonia, hepatopathy (elevated liver enzymes), and myositis (elevated creatine kinase). Diagnosis relies on serological confirmation. IgG and IgM titres should be measured at presentation, and two to four weeks later (Lappin *et al* 1989). IgM titres, indicating acute infection, are detectable seven days post-infection and return to normal after 3 - 12 weeks. Elevations in IgG titre are not detected for 10 - 14 days. A fourfold or greater elevation of the IgG titre in a three week convalescent sample suggests recent infection. The prognosis is poor, although improvement may be seen with clindamycin (25 mg/kg PO divided BID) or potentiated sulphonamide therapy (trimethoprim sulfadiazine 15 mg/kg combined BID).

Rabies virus infection may produce one of two clinical syndromes. The "dumb" form is characterised by signs of depression and rapidly progressive tetraplegia. The "furious" form manifests as erratic, aggressive behaviour, wandering, salivation, and tremors. Cats usually exhibit the furious form, which progresses to the dumb form. Definitive diagnosis is usually made post mortem by histopathological examination. Immunofluorescent testing of whisker follicles may provide ante mortem confirmation in 25-50% of infected animals (Greene 1990).

Feline meningoencephalomyelitis is an uncommon disease reported in cats three months to six years of age. Inflammatory lesions predominate in the grey matter of spinal cord, brainstem and cerebrum, producing progressive pelvic limb paresis and ataxia, behavioural changes and seizures. A viral aetiology is suspected (Lundgren 1992, Hoff and Vandevelde 1981).

Feline immunodeficiency virus (FIV) has been associated with a variety of neurological diseases where its main pathogenic role is that of immunosuppression. The full significance of FIV as a neuropathogen is not yet known, but recent investigations have identified primary CNS lesions, which include perivascular cuffing, glial nodules and diffuse gliosis in sub-cortical nuclei (Dow *et al* 1990).

Cryptococcus neoformans is the most common fungal infection of the CNS in cats. Following infection by inhalation, the organism may invade the brain haematogenously or by direct extension through the cribriform plate. Signs of intracranial disease may be accompanied by respiratory, ocular or cutaneous disease. Diagnosis is made by cytological demonstration of the organisms, culture or serology. Although the prognosis is poor, successful treatments have been reported with amphotericin B and ketoconazole.

Feline spongiform encephalopathy, newly recognised in the wake of the bovine spongiform encephalopathy epidemic, causes behavioural change (timidity or aggression), hyperaesthesia and ataxia. Clinical signs progress over several weeks and at the present time diagnosis can only be confirmed by histopathology (Gruffydd Jones *et al* 1991, Wyatt *et al* 1991).

Trauma

Head trauma may be sustained in a number of different ways, for example, road traffic accident (RTA), bite wounds, malicious injury. The degree of neuroaxonal and vascular damage varies, and the resulting neurological signs range from depression to coma. Puncture wounds carry a high risk of infection and haemorrhage.

Increased intracranial pressure (ICP) due to haemorrhage or oedema is a serious complication of many intracranial disease processes and should always be considered in animals with head trauma. Uncontrolled, elevated ICP may lead to fatal brain herniation.

Therapy depends on the severity, nature and progression of the injury, and ranges from observation to intensive medical management. The full consequences of head trauma may not be immediately evident at the time of presentation. Progressive haemorrhage or developing infection may not be apparent for several hours or days after the initial insult. Clinical signs indicating this problem include progressive locomotor dysfunction, reduced awareness, and sluggish pupillary light reflexes.

Therapeutic considerations in animals with altered consciousness include airway maintenance and oxygen supplementation, hyperventilation, judicious fluid therapy, corticosteroids, hyperosmotic and diuretic agents. Controversy exists over the benefit of corticosteroids in head injury, although most veterinary neurologists still advocate their use. Strict dose guidelines are not available, although some clinicians use a dose regime similar to that used in spinal trauma (Chapter 10). Mannitol, an osmotic diuretic, administered as a 20 % or 25 % solution at a dose of 0.5-1.0 g/kg over a three minute period should be considered in animals with severe (life threatening) signs, or a rapidly deteriorating neurological status in which elevated ICP is strongly suspected. It is best avoided in stable animals because of the possibility of potentiating intracranial haemorrhage. Frusemide (0.7 mg/kg) given IV or IM 15 minutes after mannitol infusion prolongs the effect of the mannitol (Roberts *et al* 1987). Good renal function must be established before mannitol is administered, to prevent volume overload and pulmonary oedema. Adequate respiratory function should be ensured as hypoxia and hypercapnia elevate ICP.

Post-traumatic seizures may be controlled with diazepam 0.5-1.0 mg/kg IV and / or phenobarbitone 2-6 mg/kg IV slowly. Pentobarbitone (5-15 mg/kg IV) may be used to effect in treatment of refractory seizures. Anaesthesia of animals with traumatic intracranial injuries may be a high risk procedure as lowered systemic vasomotor tone may further compromise intracranial blood flow. In the event of penetrating wounds or depression fractures with parenchymal laceration, infection and intracranial haemorrhage become significant risks and surgical intervention should be considered.

Toxins

Toxins may be accumulated by absorption through the skin, self grooming of a contaminated hair coat or direct ingestion. The most commonly incriminated toxins are the organophosphates (OP), carbamates and the chlorinated hydrocarbons, used either excessively or inappropriately as parasiticides (Dorman 1993, Dorman and Fikes 1993). Carbamates and OP act as cholinesterase inhibitors, allowing excessive synaptic activity of acetylcholine. Clinical signs are usually acute, reflecting nicotinic and muscarinic receptor overactivity and include: salivation, vomiting, diarrhoea, miosis, bradycardia, muscular tremors and convulsions. Atropine (0.2 mg/kg with 25% of the dose given IV and the remainder IM) is used to alleviate muscarinic signs of OP and carbamate toxicity. Pralidoxime (2-PAM) is indicated in OP toxicity but not in carbamate toxicity.

Chlorinated hydrocarbon toxicity is frequently associated with hyperaesthesia and convulsions in addition to many of the signs of OP toxicity. Treatment is mainly supportive.

Therapy of intoxications should always include supportive fluid therapy. Gastric lavage followed by the instillation of activated charcoal is indicated for recently ingested toxin. Bathing the animal is indicated if topical intoxication is apparent.

Prescription drugs may also result in signs of neurological disturbance if given excessively, inappropriately, or due to an idiosyncratic drug reaction.

Vascular

Cerebral ischaemic necrosis (CIN) (Feline ischemic encephalopathy), is an acute, unilateral, hypoxic insult to the forebrain (Figure 15.3). The aetiology is unknown, but thrombosis and vasculitis of cerebral vessels have been observed in some patients (Zaki and Nafe 1980). Adult cats of either sex may be affected. Clinical signs are acute, usually non progressive after the first 24 hours and may include any combination of the characteristic signs of a forebrain disorder. Focal seizure activity may produce tonic / clonic muscle contractions on one side of the head or body. The severity of clinical signs is directly related to the size of the ischaemic area. Corticosteroids may be given as described earlier for head trauma, although controversy exists over their use. Diazepam, phenobarbitone and pentobarbitone may be

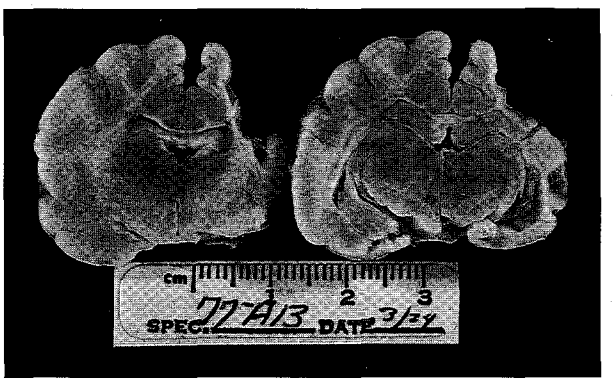


Figure 15.3: *Transverse section of the brain demonstrating destruction of the left parietal cortex following vascular compromise of that area (cerebral ischaemic necrosis). (Courtesy Dr. A. deLahunta.)*

used for seizure control. The acute signs may regress in a few days and the prognosis is usually favourable, although permanent deficits may remain. Diagnosis is often presumptive, based on history and clinical signs. Non-specific elevations of CSF protein concentration and cell counts are seen.

Systemic hypertension is being recognised with increasing frequency. Non-specific signs of forebrain disease have been reported, which improve with successful anti-hypertensive therapy (Littman 1994).

Cranial Nerve Disorders

Cranial nerves carry sensory information to and motor impulses from the brainstem (Figure 15.1). Cranial nerve dysfunction may result from disease of the peripheral cranial nerve trunk or its brainstem nucleus. Brainstem lesions are usually associated with additional findings of postural reaction deficits and mentation changes.

Pupillary abnormalities

Horner's syndrome consists of miosis, ptosis, protrusion of the third eyelid and enophthalmos due to sympathetic dysfunction (Figure 15.4). Although not a cranial nerve, sympathetic dysfunction is discussed here because of its integration in the cranial nerve examination. The most common site of injury is the middle ear in otitis media, neoplasia or trauma. A thorough otic examination and radiographs of the bullae are required. Other potential sites of sympathetic injury include the cervical spinal cord, brachial plexus and vagosympathetic trunk (Oliver and Lorenz 1993).

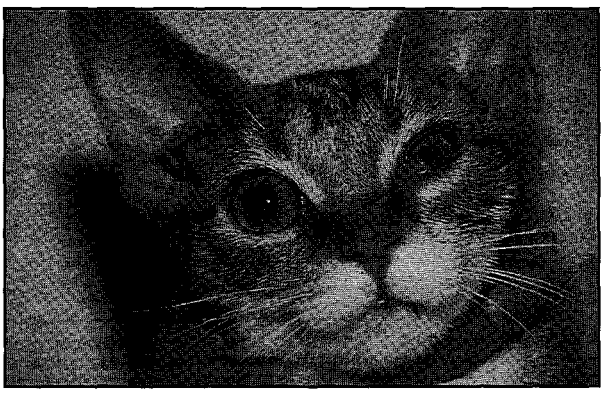


Figure 15.4: *Horner's syndrome in a cat with otitis media. Miosis, ptosis and protrusion of the third eyelid are apparent. (Courtesy Dr. NJH Sharp.)*

Feline dysautonomia may present initially as anisocoria, and progress to bilateral mydriasis and protruded third eyelids. Pupillary abnormalities may be accompanied by dry eyes, nose and mouth, regurgitation due to megaoesophagus, constipation, and dysuria due to panautonomic dysfunction (Figure 15.5). The prognosis is poor although some animals have survived with supportive care (Sharp *et al* 1984) (Chapter 11).

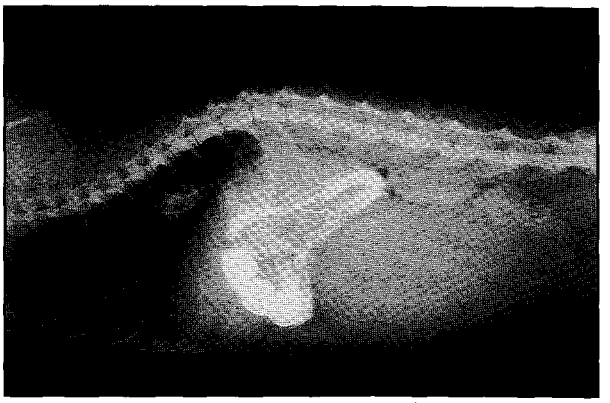


Figure 15.5: *Radiograph of a cat with feline dysautonomia demonstrating megaoesophagus, large bladder and constipation. (Courtesy Dr. NJH Sharp.)*

FeLV infection may cause anisocoria and abnormal pupillary movements through unknown mechanisms.

Thiamine deficiency

This is primarily a brainstem disorder that occurs in cats fed either a raw fish diet high in thiaminase or an overcooked diet in which the thiamine has been denatured. Chronically anorexic cats are also susceptible to the disease, particularly if they are systemically ill. The clinical signs are acute in onset and may include tetraparesis, vestibular dysfunction, pupillary abnormalities, ventoflexion of the neck, and seizures. On post-mortem examination, multifocal malacic, haemorrhagic areas are observed in the midbrain and brainstem nuclei. Treatment of thiamine deficiency includes corticosteroids to reduce oedema, and 50-100 mg thiamine administered daily IV or IM for up to a week or until the cat is eating well. If treated early a response to therapy may be seen in a few days.

Cranial Polyneuropathy

Lymphoma, metastatic carcinoma and skull base tumours may affect several cranial nerves producing multiple deficits (Figure 15.6). Diagnosis requires CSF analysis, and CT or MRI.

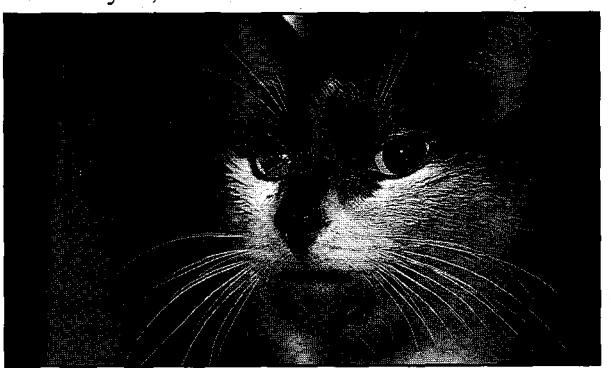


Figure 15.6: *Cranial polyneuropathy in a cat: Dropped jaw (bilateral mandibular nerves), mydriasis of the left eye (oculomotor nerve), tongue weakness (hypoglossal nerve) and protruded nictitans (sympathetic dysfunction) developed following metastasis of a mammary carcinoma to the floor of the cranial vault.*

Vestibular Disease

Head tilt and nystagmus are the hallmarks of vestibular disease, and result from lesions affecting either the peripheral (inner ear and vestibular nerve) or central (brainstem and ventral cerebellum) vestibular systems (Figure 15.7). Central lesions also produce postural deficits, hypermetria and mentation changes which aid in distinction of the two locations. Recognition of central vestibular disease should raise the suspicion of inflammatory or neoplastic disease (Chapter 2).

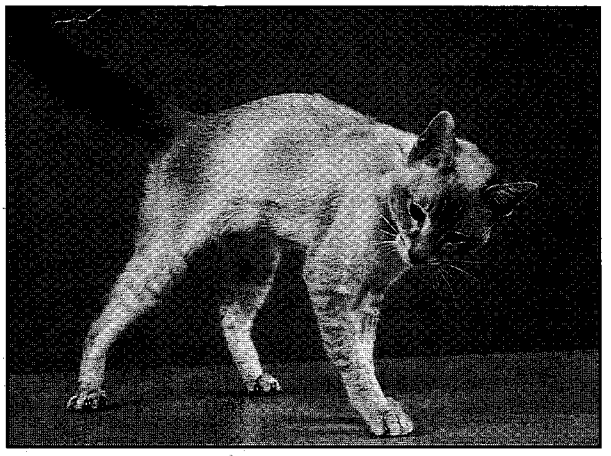


Figure 15.7: *Head tilt in a five year old siamese cat. Normal mentation, absence of other cranial nerve involvement or postural deficits indicated peripheral vestibular disease. (Courtesy Dr. CL Chrisman.)*

Otitis interna secondary to otitis media is a common cause of peripheral vestibular disease. Diagnosis requires thorough otic examination and radiographs of the tympanic bullae (Figure 15.8). In difficult cases CT or MRI may be useful to confirm the diagnosis. Facial paralysis and Horner's syndrome may accompany the head tilt. Therapy involves medical treatment, or bulla osteotomy to remove inspissated purulent debris or nasopharyngeal polyp. Antibiotic therapy alone may be unsuccessful.

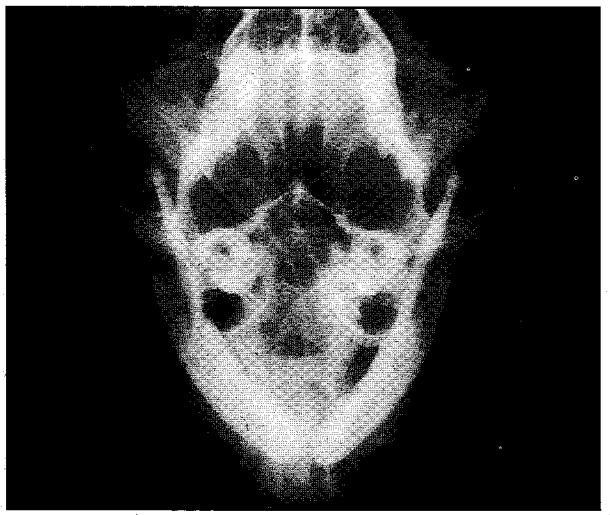


Figure 15.8: *Bulla radiographs of the cat in Figure 15.7, demonstrating osteosclerosis and increased radiodensity of the left tympanic bulla.*

Idiopathic vestibular disease is characterised by an acute onset of head tilt and nystagmus, which may be so severe as to cause incessant rolling, crying and vomiting. Although peripheral in nature, the exact location of the lesion is not known (Burke *et al* 1985). Most cases are seen in the late summer and autumn but the aetiology is unknown. Resolution of clinical signs occurs over a period of 2-4 weeks and does not appear to be influenced by either antibiotic or corticosteroid therapy. Diagnosis is made by exclusion of other diseases e.g. trauma, neoplasia and otitis media.

Aminoglycoside antibiotics (especially streptomycin) are well known causes of peripheral vestibular disease in cats.

Infectious. Any of the previously mentioned CNS infections could cause vestibular disease, with FIP virus being the most likely.

Congenital vestibular disease has been reported in Burmese and Siamese cats and may be associated with deafness (deLahunta 1983).

Deafness

The most common form of deafness is the congenital form seen in white haired, blue eyed cats. Deafness may also result from bilateral otitis media, or toxic insults from drugs such as the aminoglycosides.

Laryngeal paralysis

Laryngeal paralysis due to vagal nerve dysfunction has been reported as a cause of upper airway obstruction, dyspnoea and stridor in cats (Hardie *et al* 1981). FeLV infection has been incriminated in some cases while others are idiopathic. Partial laryngectomy may alleviate the signs.

Strabismus

The most common form of strabismus is the congenital form seen in Siamese cats.

Blindness

Fundoscopic examination and evaluation of pupillary function is essential in blind cats. Blindness with normal pupillary function suggests a forebrain lesion. Blindness with deficient pupillary function suggests a lesion in the eyes, optic nerves, optic chiasm or optic tracts. Acute blindness in cats is usually due to ocular disease (Chapter 9).

Any of the previously mentioned forebrain diseases can result in blindness. Involvement of the optic nerve, chiasm or tracts, usually related to inflammatory disease or neoplasia on the base of the cranial vault.

Systemic hypertension may cause blindness due to retinal detachment or haemorrhage. Concomitant

Table 15.2: Differential diagnosis of cerebellar signs.

Degenerative	Lysosomal storage disease, neuroaxonal dystrophy
Anomalous	Cerebellar hypoplasia
Metabolic	
Nutritional	
Neoplastic	Lymphoma, ependymoma, choroid plexus papilloma
Inflammatory	FIP, Toxoplasma, meningoencephalomyelitis
Idiopathic	
Toxic	
Traumatic	Road traffic accident, bite
Vascular	

neurological signs may occur, possibly due to intracranial haemorrhage (Littman 1994).

Ataxia of the Head and Limbs (Table 15.2)

Incoordination of the head, neck and all four limbs is most often an indication of **cerebellar disease**. Other typical signs include intention tremor of the head, hypermetria, normal conscious proprioception, and menace deficits with normal vision.

Degenerative

Lysosomal storage diseases. (See above) Cerebellar dysfunction is common in cats with lysosomal storage diseases and is often accompanied by signs of cerebral involvement. Suspicion of this aetiology arises from the clinical signs, progressive nature, and signalment. Diagnosis is based on enzyme analysis of fibroblast cultures.

Anomalous

Cerebellar hypoplasia is caused by intrauterine or peri-natal infection with the feline panleucopenia virus, which causes cell destruction at the time of cerebellar development (Figure 15.9). The clinical signs of hypermetria, wide based stance, whole body and head sway, and intention tremor of the head, become apparent at the onset of ambulation and are non-progressive. Affected cats may make perfectly good pets.

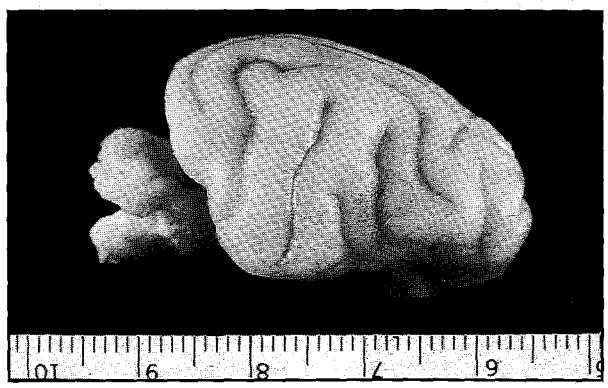


Figure 15.9: *Cerebellar hypoplasia due to in utero infection with feline infectious peritonitis virus. (Courtesy Dr. JN Kornegay.)*

Paraparesis, Paraplegia (Table 15.3)

Weakness (paraparesis) or absence (paraplegia) of pelvic limb movement implies a lesion of one of the following (Figure 15.10):

- the spinal cord caudal to the thoracic limb outflow of C_6-T_2
- the peripheral nerves supplying the pelvic limbs
- the pelvic limb vascular supply

Degenerative

Disc protrusions are a surprisingly common post mortem finding in cats, but rarely cause clinical problems. If present, clinical signs include chronic progressive paraparesis and pain.

Table 15.3: Differential diagnosis of paraparesis / paraplegia.

Degenerative	Lysosomal storage disease (mucopolysaccharidosis)
Anomalous	Spina bifida
Metabolic	
Nutritional	
Neoplastic	Lymphoma
Inflammatory	FIP, Toxoplasma, meningoencephalomyelitis
Idiopathic	
Toxic	
Traumatic	RTA, disc herniation
Vascular	Aortic thromboembolism

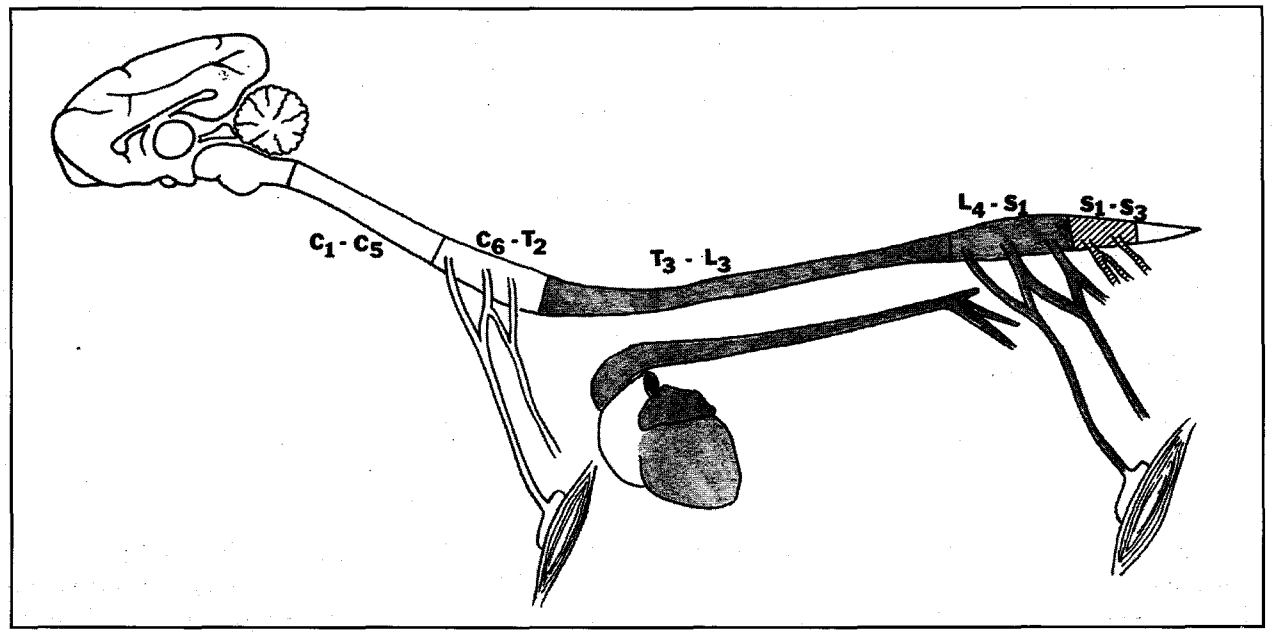


Figure 15.10: Diagrammatic representation of lesion localisation for diseases causing: Paraparesis / paraplegia (shaded area) and micturition disorders (hatched area).

Neoplasia

Extradural lymphoma is the most common spinal tumour in cats (Wheeler 1989). Young adult cats (3 - 4 years of age) are most often affected. Most neoplasms are located in the thoracolumbar area causing progressive pelvic limb dysfunction and spinal pain (Figure 15.11). Less commonly, cervical lesions result in tetraparesis, while meningeal and peripheral nerve involvement cause signs of lower motor neuron dysfunction. Clinical signs develop over three days to three weeks. Other systemic signs of FeLV infection are often present. Lymphoblastic infiltration of the bone marrow is found in 67% of cases. FeLV testing of the serum is positive in 84-100% (Spodnik *et al* 1992; Lane *et al* 1994). Confirmation of the location and nature of the lesion requires myelography, and possibly surgical or fluoroscopically guided needle biopsy. The long term prognosis is poor but temporary remissions (4-5 months) may be obtained using combinations of corticosteroid, chemotherapy and radiation therapy. The nervous system is affected in about 5-10% of cats with lymphoma, and the spinal cord is affected with much greater frequency than the brain.

FeLV infection has also been associated with proliferative bony lesions (osteochondromas) of the ribs, spine, skull and limb bones. Lesions may be single or multiple and tend to cause pain and compress adjacent structures. Young adult cats are affected and malignant transformation to osteosarcoma may occur (Pool 1981). Other spinal tumours are rare in cats.

Inflammatory disease

FIP virus, Toxoplasma gondii, and non-suppurative meningoencephalomyelitis have been previously mentioned as causes of focal and multi-focal CNS lesions. Signs of focal spinal cord disease may occur but are often accompanied by signs of intracranial disease (e.g. seizures) or ocular involvement suggesting systemic disease, or both.

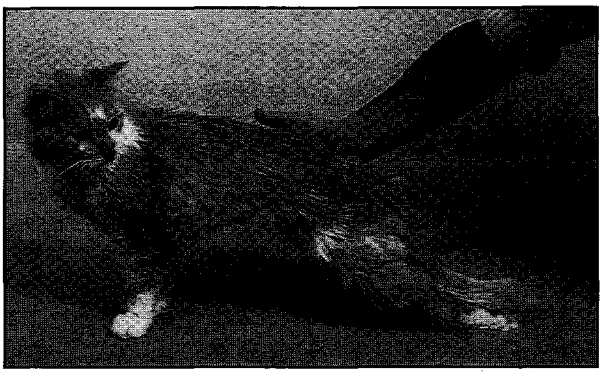


Figure 15.11: Paraplegia due to spinal lymphoma in a three year old domestic short hair cat. Differential diagnoses include, trauma, myelitis (FIP, Toxoplasma), aortic thromboembolism and intervertebral disc disease.

In the early stages, rabies may also present with non-specific signs such as paraparesis (Fogelman 1993).

Trauma

Traumatic spinal injuries may vary from cord contusion alone to grossly distracted spinal luxations or fracture luxations with severance of the spinal cord. Prognosis and treatment are based on assessment of the site and severity of the injury and radiographic findings. These are discussed further in Chapter 10.

Vascular

Ischaemic neuromyopathy ("aortic embolism", "saddle thrombus") of the pelvic limbs follows embolic

Table 15.4: Neuromuscular causes of tetraparesis / tetraplegia

Degenerative	Hypertrophic muscular dystrophy, Devon Rex myopathy Nemaline myopathy
Anomalous	
Metabolic	Diabetes mellitus, hyperthyroidism Hypokalaemia, hypernatraemia, hypocalcaemia
Nutritional	
Neoplastic	Lymphoma
Inflammatory	Immune mediated polyneuritis \ polymyositis Myasthenia gravis, Toxoplasmosis
Idiopathic	
Toxic	OP, Lead
Traumatic	
Vascular	

occlusion of the aortic trifurcation. Affected cats suffer acute paraparesis or paraplegia associated with cold limbs, absent femoral pulses, cyanotic nail beds and later stiff, painful, pelvic limb muscles (Griffiths and Duncan 1979). Paresis may be associated with a plantigrade stance. The patellar reflexes are often intact, whilst hock flexion and pain sensation in the toes are diminished or absent. Occasionally a thoracic limb may be affected. Serum CK concentrations are usually elevated because of hypoxic damage to the muscles. The thrombus is thought to originate in the dilated left atrium of cats with various forms of cardiomyopathy. The prognosis is guarded because of the underlying condition and potential for re-embolization, but therapy with aspirin, heparin, acepromazine and thrombolytic agents may be considered (Pion and Kittleson 1989). Appropriate steps should be taken to manage the cardiac disease.

Tetraparesis, Tetraplegia (Table 15.4)

Synonymous with quadriparesis and quadriplegia these terms imply weakness (-paresis) and absence (-plegia) of movement in all four limbs. Tetraparesis may result from lesions affecting the following (Figure 15.12):

- brain
- cervical spinal cord
- the neuromuscular system

Brain lesions causing tetraparesis are usually associated with other signs of intracranial disease, for example, seizures, altered mentation and behaviour. These diseases have been covered previously and will not be discussed here.

Spinal Cord Disorders

The neoplastic, inflammatory and traumatic lesions

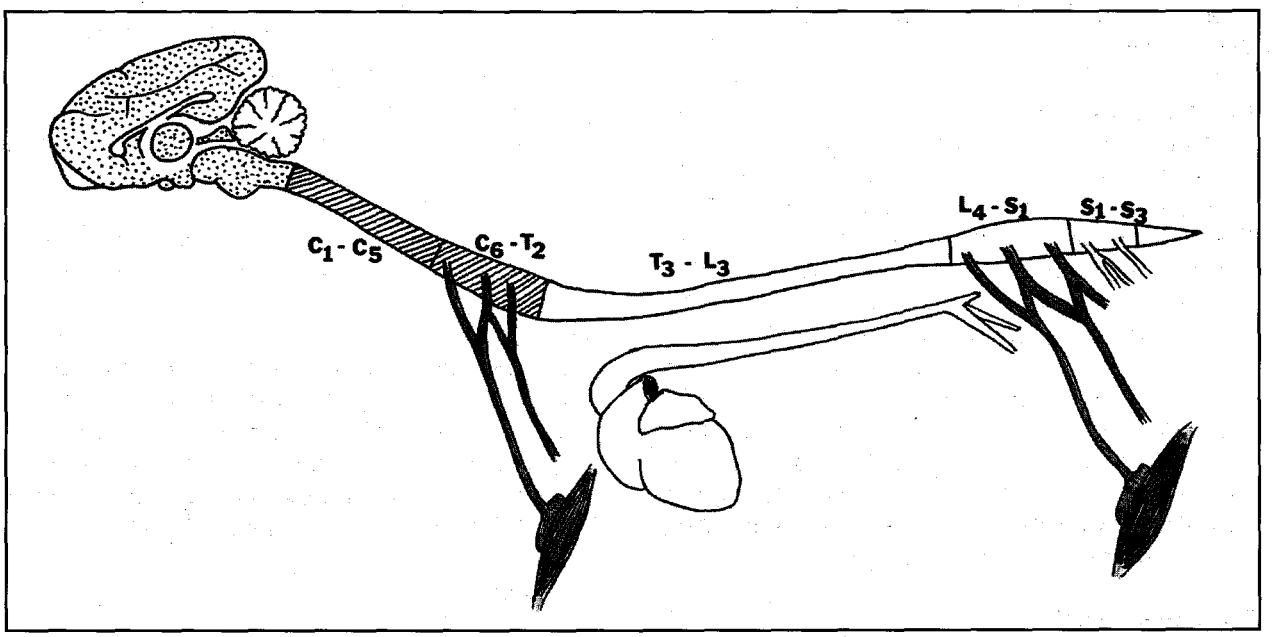


Figure 15.12: Diagrammatic representation of lesion localisation for diseases causing tetraparesis; (a) Forebrain and brainstem (dotted area), (b) cervical spinal cord (hatched area), and (c) neuromuscular system (shaded area).

discussed previously can affect the cervical spinal cord resulting in tetraparesis or tetraplegia.

Atlantoaxial subluxation has been reported in cats (Jaggy *et al* 1991; Shelton *et al* 1991) (Chapter 10).

Hypervitaminosis A results in extensive bone proliferation around diarthrodial joints, especially in the spine. Neurological deficits result from compression of the spinal cord.

Neuromuscular disorders

The neuromuscular system is composed of the peripheral motor neuron, neuromuscular junction and muscle cell. Diseases of these components may be termed neuropathy, junctionopathy and myopathy respectively. Clinical signs are diffuse and may be progressive or episodic. Weakness may be more apparent in the pelvic limbs so critical evaluation of the thoracic limbs is important to establish the diffuse nature of the disease. A common clinical sign of neuromuscular weakness is ventral flexion of the neck (Figure 15.13).

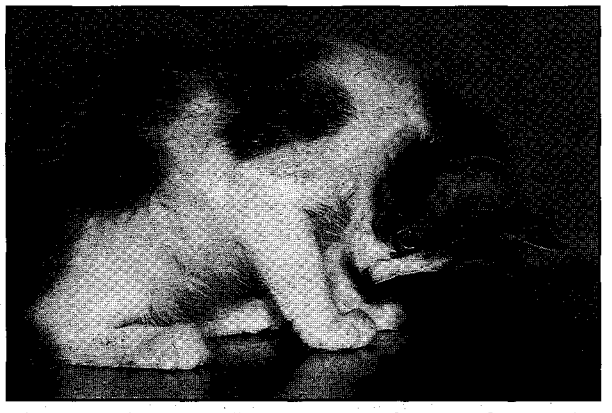


Figure 15.13: *Ventral flexion of the neck is an indicator of neuromuscular weakness. Differential diagnoses include hypokalaemia, chronic OP intoxication, myasthenia gravis, hyperthyroidism and polyneuropathy.*

(i) Neuropathy (Chapter 14)

Diabetes mellitus. The best known peripheral neuropathy of cats is that caused by diabetes mellitus. Affected cats have a characteristic plantigrade stance in the pelvic limbs due to sciatic neuropathy (Figure 15.14). Varying degrees of postural deficits, muscle atrophy, weak reflexes and decreased muscle tone are found. Critical evaluation of the thoracic limbs reveals similar but often less apparent findings. The clinical signs often improve with management of the diabetic state.

Primary inflammatory polyneuritides are rare but may be responsible for signs of acute or chronic diffuse lower motor neuron dysfunction characterised by varying degrees of weakness, muscle atrophy, postural deficits and decreased reflexes (Malik *et al* 1991). Improvement of the signs may occur with corticosteroid administration.

Figure 15.14: *Plantigrade stance in the pelvic limbs due to sciatic neuropathy. This stance is characteristic of diabetic neuropathy, but also may be seen in animals with aortic thromboembolism and lymphomatous infiltration of the pelvic nerves.*

(ii) Junctionopathy (Chapter 13)

Myasthenia gravis is an exercise induced weakness resulting from a deficiency of acetylcholine receptor in the post-synaptic membrane. In most instances this is due to immune-mediated attack of the acetylcholine receptor, but congenital deficiency has been reported (Indrieri *et al* 1983). Clinical signs often manifest as progressive stiffness of the gait and collapse with cervical ventroflexion (Joseph *et al* 1988). Megaoesophagus may result in aspiration pneumonia and signs of respiratory distress. Thymomas have been associated with this condition in cats (Scott-Moncrieff *et al* 1990; O'Dair *et al* 1992). Diagnosis is made on the basis of a response to intravenous edrophonium (0.05-0.1 mg/kg IV), electrodiagnostic testing and detection of antibody to the acetylcholine receptor. Treatment with pyridostigmine (2 mg/kg PO BID) and corticosteroids may result in clinical improvement (Cuddon 1989).

Clinical signs of ***organophosphate (OP) intoxication*** include generalised weakness with muscle fasciculations, autonomic overactivity and seizures. Fenthion acts in a similar way to other OP but produces a different clinical picture, in that muscle tremors and profound weakness predominate without parasympathetic dysfunction (Nafe 1988). Cervical ventroflexion is a common clinical sign. Diphenhydramine has been used to reverse the nicotinic signs (Clemmons *et al* 1984). Diagnosis of OP intoxication is based on the clinical signs, history and low serum cholinesterase concentrations.

(iii) Myopathy (Chapter 13)

Muscle diseases may be associated with any of the following abnormalities; pain, pyrexia, muscle atrophy, gait abnormalities, generalised weakness, raised serum CK concentrations, and ventroflexion of the neck. Definitive diagnosis often requires serological, electrophysiological and muscle biopsy evaluation.

Table 15.5: Differential diagnosis of monoparesis / monoplegia

Degenerative	
Anomalous	
Metabolic	Hyperchylomicronaemia
Nutritional	
Neoplastic	Lymphoma
Inflammatory	
Idiopathic	
Toxic	Tetanus
Traumatic	Road traffic accident, surgery,
Vascular	Thromboembolism, tourniquet

Muscular dystrophy. Although rare, the number of muscular dystrophies reported in cats is steadily increasing. These include feline hypertrophic muscular dystrophy characterised by stiff movements and muscle hypertrophy (Gaschen *et al* 1992), Devon Rex hereditary myopathy characterised by atrophy and ventroflexion of the neck (Malik *et al* 1993) and nemaline myopathy characterised by weakness, atrophy and muscle trembling (Cooper *et al* 1986).

Polymyositis is rare and reported as an idiopathic, suspected autoimmune disorder, or in association with *Toxoplasma* infection.

Electrolyte disturbances may result in profound alterations in neuromuscular activity.

Hypocalcaemia causes weakness and muscular tremors.

Hypokalaemia is well recognised as a cause of polymyopathy associated with generalised weakness, ventroflexion of the neck, and raised CK concentrations (Dow *et al* 1987). Potassium depletion may result from decreased intake, gastrointestinal losses, renal losses (e.g. renal disease, diabetes mellitus) or cellular ionic shifts (e.g. alkalosis).

Hypernatraemia has also been reported as a cause of muscle weakness (Dow *et al* 1987).

Hyperthyroidism has also been associated with diffuse weakness. Although the underlying mechanism is unclear, return to a euthyroid state is accompanied by resolution of signs (Joseph and Peterson 1992)

Monoparesis, Monoplegia (Table 15.5) (Chapter 11)

Metabolic

Hyperchylomicronaemia is an hereditary defect in lipid metabolism resulting in lipid granuloma formation and compression of adjacent structures. Peripheral nerve deficits have been reported in association with this condition (Jones 1993)

Neoplasia

Peripheral nerves can be affected by primary neoplasms (e.g. neurofibroma), compressed by adjacent neoplasms, or infiltrated by neoplastic cells (e.g. lymphoma). In addition to lower motor neuron signs, paraesthesia may cause the animal to lick and traumatise the skin of the appropriate sensory field.

Toxic

Although cats are regarded as resistant to tetanus, several cases of tetany localised to one limb have been reported in association with draining wounds (Malik *et al* 1989). Treatment with antibiotics and muscle relaxants may effect a recovery over several weeks.

Trauma

Peripheral nerve injury results from a variety of mechanisms such as RTA, fractures, luxations, bites, and surgery. The nature of the injury also varies, e.g. compression, stretch, laceration and avulsion. The prognosis depends on the degree of axonal disruption. Nerve root avulsion carries the worst prognosis with regeneration extremely unlikely. Laceration also carries a poor prognosis, unless the severed ends can be surgically reapposed. In stretch and compressive injuries, recovery times vary from a week to several months. Demyelination is rapidly repaired, but axonal disruption requires regeneration, which takes place at a rate of 1 - 2 mm per day. As peripheral nerves are mixed, sensory and motor deficits are observed.

Vascular

Although pelvic limb dysfunction is the most common neurological sequel to cardiomyopathy, emboli occasionally lodge in a thoracic limb artery producing a similar constellation of signs.

Overzealous applications of limb restraints and tourniquets can produce ischaemia and crush injuries to peripheral nerves with resultant deficits. Recovery may take several days to weeks depending on the severity of the injury.

Table 15.6: Differential diagnosis of urinary disorders

Degenerative	Feline dysautonomia
Anomalous	Sacrocaudal dysgenesis (spina bifida)
Metabolic	
Nutritional	
Neoplastic	Lymphoma
Inflammatory	FIP, toxoplasmosis, bite wound
Idiopathic	
Toxic	
Traumatic	Lumbosacral trauma
Vascular	

Micturition Disorders (Table 15.6) (Chapter 12)

Degenerative

Feline dysautonomia is often associated with a large, atonic bladder and dysuria. Constipation may also be noted.

Anomalous

Spina bifida is the most common developmental abnormality of the feline spinal cord (Deforest and Basrur 1979). The term implies failure of closure of the vertebral arches, which may occur alone or in conjunction with varying degrees of meningeal and spinal cord dysplasia. A weeping tract may be observed in the dorsal lumbar skin. Manx cats are most commonly affected by this condition. Severely affected animals show signs of cauda equina dysfunction, which may include a plantigrade pelvic limb stance, dilated areflexic anus, large easily expressed bladder, and faecal and urinary incontinence. Soiling of the perineum may be associated with urinary tract infections.

Trauma

Sacrocaudal fracture / luxation. Characteristic signs are seen in cats sustaining injury to the sacrocaudal spine. These may be grouped, in order of increasing severity:

- a paralysed tail alone
- a distended bladder that is difficult to express and which the cat continually strains to empty
- a distended bladder that cannot be expressed but which causes the animal no distress
- a flaccid, atonic bladder with continual overflow and an areflexic anus

(Moise and Flanders 1983).

Radiographic abnormalities in these animals may be minimal (Smeak and Olmstead 1985). Clinical signs are thought to be due to differing degrees of traction injury to the caudal, pudendal and pelvic nerves. With appropriate nursing the prognosis for the first two groups is good, the third poor and the last, grave. Cats that regain continence usually do so within a month. Tail paralysis may necessitate amputation.

Self Mutilitation Syndromes

Hyperaesthesia (increased sensitivity to tactile and painful stimuli) and paraesthesia (spontaneous abnormal sensations) are abnormal sensory phenomenon that may result in self mutilation behaviour ranging from excessive licking to autoamputation. Consideration should be given to a structural or active disease process (neoplasia, trauma, diabetes mellitus, inflammation) producing sensory irritation.

Trauma

Nerve root avulsion or ***peripheral nerve trauma*** may lead to self mutilation because of the action of inflammatory mediators around exposed axons.

Idiopathic

Feline hyperaesthesia syndrome is characterised by varying degrees of apparent irritation of the dorsal thoracolumbar area. Clinical presentation ranges from rippling of the skin to chewing of the hair and skin and screaming when touched. No cause has been ascertained. Treatments tried with varying degrees of success include, phenobarbitone, prednisone and megestrol acetate.

Inflammatory

Hyperaesthesia has been reported in association with feline spongiform encephalopathy and non-suppurative meningoencephalomyelitis.

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CHAPTER SIXTEEN

Neurological Problems of Exotic Species

Martin P.C. Lawton

INTRODUCTION

The fact that an animal is exotic does not preclude it from suffering neurological problems similar to those seen in dogs, cats, and other domestic animals.

Presentation of an exotic animal often causes a mental block for many veterinarians, but by applying first principles, there is no reason why the cause of a neurological deficit in any such animal cannot be investigated. In addition to general principles, an understanding of the dietary requirements of exotic animals is also beneficial.

Exotic animals may be divided into mammals, birds, and ectotherms (poikilotherms).

The ectotherms include reptiles, fish, and invertebrates. The distinction is not just of academic interest, but is also of practical importance.

Mammals and birds are able to regulate their body temperature (endotherms) and respond in a standard way when examined. Those animals whose metabolism is affected by the external temperature (ectotherms) may show different clinical signs at different temperatures.

Similarly, reflexes also vary at different temperatures, because of metabolic effects on the speed of conduction of impulses through the nervous system.

Ectotherms may also undergo hibernation if the external temperatures falls too far below their preferred body temperature, causing their bodily responses to be diminished or to become virtually absent. However, even a tortoise that is in hibernation will move the forelimb in response to gentle stroking of that limb, albeit very slowly. Problems may arise for the inexperienced practitioner in assessing whether or not an ectotherm is alive or brain dead, a distinction most easily established by trying to return it back to its preferred body temperature by gradually increasing the temperature.

Neurological problems of exotics may be divided into those resulting from the following: diet, environment, toxicity, or trauma.

Traumatic problems are usually associated with incorrect handling, or with too much "furniture" and toys in the cage, resulting in crush injuries.

FERRETS

Ferrets may show neurological problems similar to those described for the dog and cat, but are particularly prone to parvovirus (Aleutian disease), botulism, and canine distemper. Any ferret showing hind limb paresis or weakness should be investigated for evidence of Aleutian disease.

Aleutian disease

This parvovirus infection is the commonest cause of hind limb ataxia and paresis, or even tetraplegia in

Table 16.1: *Causes of possible neurological problems in ferrets.*

Ataxia	Abscessation Aleutian disease Botulism
Paresis	Aleutian disease Botulism Trauma
Seizures	Canine Distemper Dehydration Liver disease Rabies Renal failure

domestic ferrets (Oxenham 1991; Welchman et al 1993). The infection may be persistent and there can be carriers that are free of signs. Diagnosis in on high antibody levels or histopathology of the spinal cord. Therapy can be attempted, but the prognosis is poor. There appears to be no protection given by using canine or feline parvovirus vaccines (Oxenham 1991).

Botulism

This may be seen in ferrets that are fed a raw meat diet, which has been contaminated at some stage with botulin toxin. The ferret is moderately susceptible to toxin types A and B, but highly susceptible to type C (Andrews and Illman 1987). Clinical signs, which start within twelve hours of ingestion of the contaminated food, initially are due to muscular stiffness and incoordination. However, with time and progression of the disease, the ferret becomes ataxic and eventually paralysed. Paralysis of the respiratory muscles is fatal. Treatment may be attempted with antitoxin and supportive therapy, but the outcome depends on the amount of toxin ingested and how quickly the treatment is instigated.

Canine distemper virus

Ferrets are extremely susceptible to canine distemper virus infection (Cooper 1985; Davidson 1986; Andrews and Illman 1987; Oxenham 1991). Mortality rates related to canine distemper virus infections are very high, and the course of the disease is similar to that seen and described in the dog (Cornwell 1984). If the ferret survives the initial systemic phase, then neurological signs may be seen, which are similar to that of myoclonus in the dog (Cooper 1985). There is no specific treatment, other then general nursing care and supportive therapy.

PRIMATES

It is difficult to assess all but the most severe neurological problems in primates, because of the problems in performing an adequate neurological examination safely and without the use of sedation.

Dietary problems

Primates, like birds and reptiles, are often fed an unsuitable and deficient diet, which results in prob-

Table 16.2: *Causes of possible neurological problems in primates.*

Ataxia	Encephalitis (bacterial / viral) Nutritional osteodystrophy
Paresis	Excercise restriction Nutritional osteodystrophy Poliomyelitis Trauma
Seizures	Dehydration Handling *Herpesvirus simiae* Hypocalcaemia Idiopathic epilepsy Liver disease Rabies Renal failure Stress
Ataxia	Arthritis *Encephalitozoon cuniculi* Nutritional osteodystrophy Pasteurellosis
Paresis	*Encephalitozoon cuniculi* Excercise restriction Nutritional osteodystrophy Spinal fracture *Toxoplasma gondii* Trauma
Seizures	Dehydration *Encephalitozoon cuniculi*

lems related to calcium and phosphorous imbalance and lack of vitamin D. In addition to this they also have a dietary requirement for vitamin C.

Nutritional osteodystrophy in pet primates leads to incoordination, weakness, inability to grip, and sometimes ataxia or paralysis. Radiography will often show the obvious osteodystrophy, often with secondary "pathological" fractures (Figure 16.1).

Figure 16.1: *Squirrel monkey showing severe osteodystrophy and secondary "pathological" fractures.*

Treatment is aimed at the correction of the dietary imbalance and deficiencies by changing to an adequate diet, and the use of vitamin and mineral supplementation, such as Arkvits or ACE-High (Vetark).

Seizures

Seizures in primates may be associated with osteodystrophy or true idiopathic epilepsy. Nelson (1979) reports the stress of handling as a cause of seizures. This is usually seen in juveniles and young adults, and is reproducible upon repeated conditions and handling. Treatment with anticonvulsants may by attempted.

Paralysis

Paralysis seen in primates often is accompanied by atrophy and contraction of the affected muscles, preventing them from straightening their limbs. This often is a result of inadequate cage size, and is referred to as cage paralysis. Bad injection technique may cause nerve damage (Nelson 1979). This can be avoided by giving intramuscular injections into the quadriceps, triceps or forelimb musculature.

Paralysis associated with osteodystrophy may be caused by "pathological" fracture or collapse of the vertebral column.

Other disorders

Other causes of neurological problems include rabies, poliomyelitis, or bacterial/viral encephalitis. *Herpes virus simiae* infection may result in parietal lobe atrophy and neurological disorders in infant old world primates (Brack and Gatesman 1989).

RABBITS

Neurological problems seen in rabbits are usually associated with infection or trauma.

Pasteurellosis

Torticollis is a common presenting clinical sign, often associated with otitis media or interna, or encephalitis. The affected rabbit may have a slight head tilt or it may be so severe that balance is totally disrupted. Any attempt to handle or disturb the animal will result in it spinning, and this is especially noticeable if it panics. Nystagmus also may be present.

The usual cause of otitis media and interna is *Pasteurella multocida* (Harkness and Wagner 1989, Flecknell 1991a). As well as a cause of respiratory problems, *Pasteurella multocida* is found frequently in the nares, conjunctiva, lung or pharynx but usually does not cause clinical signs (Harkness and Wagner 1989). If the organism migrates via the Eustachian tube it may result in otitis media, which eventually progress to otitis interna.

Treatment is generally ineffective (Flecknell 1991a), but may be attempted with corticosteroids and a suitable antibiotic, such as tylosin, oxytetracyline or enrofloxacin, which may result in some remission.

Encephalitozoonosis

This is caused by the parasite *Encephalitozoon cuniculi*, which affects the central nervous system (CNS) and kidneys. Occasionally it may be a cause of torticollis, paresis, or convulsions, but most cases are chronic and subclinical (Harkness and Wagner 1989; Flecknell 1991a).

Toxoplasma gondii

This may cause clinical disease in domestic rabbits (Flecknell 1991a). Clinical signs include paralysis or convulsions, and are usually followed by death in a few days. Diagnosis is at post mortem examination.

Spinal fractures

Fractures of the lumbar spine are common in rabbits (Baxter 1975), usually because the rabbit has been dropped or it struggled during restraint and handling

(Harkness and Wagner 1989; Flecknell 1991a). The resulting degree of paresis or paralysis depends on the severity and location of the damage. Radiography is useful in making the diagnosis, but total recovery is unlikely. If there is contusion to the spinal cord in the absence of a fracture, then corticosteroid treatment together with cage rest and general nursing, may be helpful.

Arthritis

Severe arthritic change may also be seen clinically and may appear to be causing a neurological deficit. Usually there is total fusion of the joint associated with the arthritis, resulting in an inability to use the offending limbs properly, and is particularly noticed if it involves the hip joint (Figure 16.2).

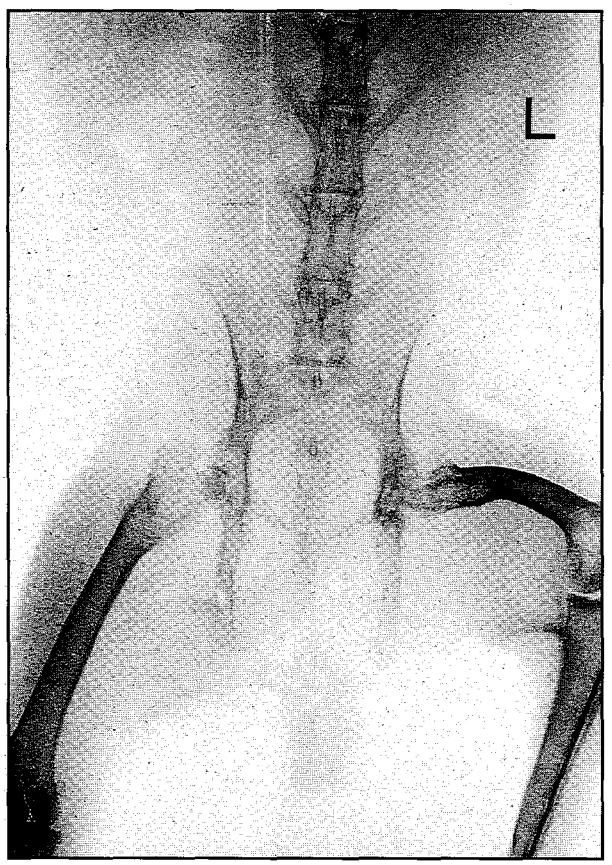

Figure 16.2: Radiograph of rabbit's hips showing severe arthritis of the left hip.

RATS AND MICE

Pasteurellosis

As in rabbits, torticollis may be exhibited and may be related to pasteurellosis (Flecknell 1991b), or a mycoplasmal infection. Treatment may be successful after prolonged course of antibiotics, such as tylosin, tetracyclines or enrofloxacin.

Lymphocytic choriomeningitis (LCM Virus)

Lymphocytic choriomeningitis can affect mice, guinea pigs, chinchillas, canines, primates, hamsters, and humans. In humans it may cause a fatal meningitis or influenza-like signs. Fortunately, the fatal meningitis is rare.

Although the natural host is the wild rodent population (Harkness and Wagner 1989), lymphocytic choriomeningitis does not usually cause signs in mice (Flecknell 1991b), but may cause hind limb paralysis.

Any rodent showing signs of a CNS disorder should be sampled for serological evidence of lymphocytic choriomeningitis in view of the public health hazard.

Trauma

Traumatic injury in these small rodents is a common occurrence, usually as a result of being dropped by young owners, causing damage to the hind limbs, spinal cord, concussion or intracranial damage. Radiographs are required to diagnose or rule out these problems. The use of dental or non-screen films are advised. It is difficult to obtain good radiographs when rare earth plates are used, as most radiographic machines have mAs and Kv too high for these small animals, unless the focal distance is drastically increased.

Other disorders

Other viral causes of neurological problems include mouse encephalomyelitis virus, mouse hepatitis virus, and mouse poliomyelitis. Inheritable neurological disorders have also been described (Mullink 1979). Radiculoneuropathy (spinal nerve root disease) is a common finding in aged rodents, as are spondylosis and arthritis, all of which can result in hind limb weakness and/or ataxia and should be ruled out by clinical examination and radiography.

GERBILS

Neurological problems discussed under rats and mice also occur in gerbils, although gerbils are more prone to spinal and hind limb injuries, as they have no concept of height and readily leap (Toy 1985a). Gerbils are particularly prone to Tyzzer's Disease (*Bacillus piliformis*). This usually causes death from hepatitis, but neurological signs related to encephalitis have been reported in naturally occurring infections.

Gerbils have one peculiarity that requires special mention. They may suffer epileptiform seizures which are provoked by handling, change of environment, or loud noises (West 1991a). It is though that the epileptiform seizures affect 20% of the gerbil population (Toy 1985a; Harkness and Wagner 1989), and are genetically influenced and thought to be a normal defensive mechanism against attack (Harkness and Wagner 1989).

These seizures vary from a mild hypnotic state to a severe myoclonic convulsion, followed by tonic extensor rigidity, which may last from 30 seconds to 2 minutes. The seizures can be very distressing to a young owner and control can be attempted by using anticonvulsant therapy, although assessing a correct dose is difficult (Toy 1985a; Harkness and Wagner 1989).

HAMSTERS

The neurological problems described for rabbits and rodents affect hamsters and include problems related to toxoplasmosis, nosematosis, bacterial otitis media/interna or encephalitis (Sebesteny 1979; Harkness and Wagner 1989).

Lymphocytic choriomeningitis has been reported in hamsters (Sebesteny 1979; Toy 1985b; Harkness and Wagner 1989) and is of concern because of the popularity of these species as pets. Lymphocytic choriomeningitis can result in incoordination or paralysis (Harkness and Wagner 1989), but may not cause clinical signs (Toy 1985b; West 1991b). The virus is excreted in the urine and saliva, thus general hygiene is an essential part of preventing the spread of this zoonosis.

Paralysis

Causes of paralysis include:-

Age - because of the lack of exercise and a small cage (Toy 1985b). Moving the hamster to larger quarters and allowing it to exercise may bring about an improvement in this condition provided it is not too advanced.

Muscular dystrophy is a genetic problem causing a hind limb paralysis, mainly of males, in the age group of 6-10 months, although it is occasionally seen in females (Caulfield 1972; Toy 1985b) (Figure 16.3).

Table 16.3: Causes of possible neurological problems in rodents.

Ataxia	Abscessation Arthritis Constipation Dystocia Enterotoxaemia Lymphocytic choriomeningitis Pasteurellosis Pododermatitis Pregnancy toxaemia (guinea pigs) Spondylosis Trauma Vitamin C deficiency (guinea pigs) Vitamin E deficiency (hamsters)
Paresis	Back strain (obese guinea pigs) Excercise restriction Lymphocytic choriomeningitis Muscular dystrophy (hamsters) Radiculoneuropathy Spinal fracture Spondylosis Trauma Vitamin E deficiency
Seizures	Dehydration Encephalomyelitis virus Enterotoxaemia Epileptiform (gerbils) Mouse hepatitis virus Mouse poliomyelitis Pregnancy toxaemia (guinea pigs) Trauma Tyzzer's disease "Wet tail" (hamsters)

Figure 16.3: Hamster with hindlimb paralysis associated with muscular dystrophy.

Vitamin E deficiency (Granodos 1968).

Miscellaneous problems - such as falls, constipation, dystocia, or infected bite wounds have also been reported (Toy 1985b).

Sleeper disease

This is a state of immobility, which is found when the temperature exceeds 22°C (Toy 1985b). The hamster, when faced with this high temperature, becomes listless, may tremble or shake, and ataxia may be the final result. When the hamster is placed in a more suitable environment normal behaviour will return.

Hibernation

This occurs when the external temperature drops below 5°C, and the hamster may be thought by their owners to be dead when in this state. The pulse and breathing are usually imperceptible and the hamster may also appear stiff and cold on handling. Any suspected "dead" hamster should always be warmed to see if it awakens.

GUINEA PIGS

Guinea pigs suffer from similar neurological problems to those described above for other rodents. Most common are otitis interna and fractured spines (Wagner 1979; Harkness and Wagner 1989). Other problems include pododermatitis, enterotoxaemia and encephalopathies.

In addition there are three problems in guinea pigs, which warrant further mention.

Pregnancy toxaemia

Pregnancy toxaemia is seen in obese sows carrying twins or a single large baby and nearing parturition. The clinical signs may vary from anorexia with incoordination to convulsions. Treatment is by caesarean section accompanied by supportive treatment with fluids and corticosteroids.

Vitamin C deficiency

Guinea pigs are unable to manufacture their own vitamin C, therefore requiring a constant dietary source. Hypovitaminosis C may result in neurological signs associated with the inability to move, or ataxia due to the swelling of the joints caused by this disease. Treatment is with vitamin C supplementation and a higher quality diet.

Back strain

Because the size and weight of pet guinea pigs, which are often obese, back strain related to incorrect handling may be seen. Harkness and Wagner (1989) have reported this problem in laboratory guinea pigs, where there is oedema and haemorrhage around the spinal cord. Clinical signs range from pain on movement to temporary paralysis.

Treatment is with strict rest. Use of corticosteroids and diuretics, although debatable, may be considered. Training of owners in how to handle these creatures may prevent further distress.

BIRDS

Neurological problems in birds may be due to dietary causes, toxins, trauma, or infections.

Calcium: phosphorus: vitamin D_3 imbalance

Inadequate diets, particularly those high in seeds such as sunflower, are very low in calcium but high in oils and phosphorus and metabolic bone disease is a common finding (Fowler 1986; Lawton 1988a). Inadequate dietary calcium or vitamin D_3 may result in a fall in the blood calcium levels and result in hypocalcaemic tetany (Fowler 1986; Coles 1988). Affected birds initially appear weak and drowsy, or sway on their perch. There may be fluttering or uncontrollable flapping of the wings (Figure 16.4).

Startling such a bird may cause a seizure, as the hypocalcaemic bird is often hyperaesthetic. Seizures may last anything from fifteen seconds to several minutes, after which the bird will be weakened and unable to climb back onto its perch, laying exhausted at the bottom of the cage. A bird in this condition, if untreated, may die rapidly.

Treatment is with intravenous or intramuscular injection of calcium borogluconate, 0.6 mg/kg giv-

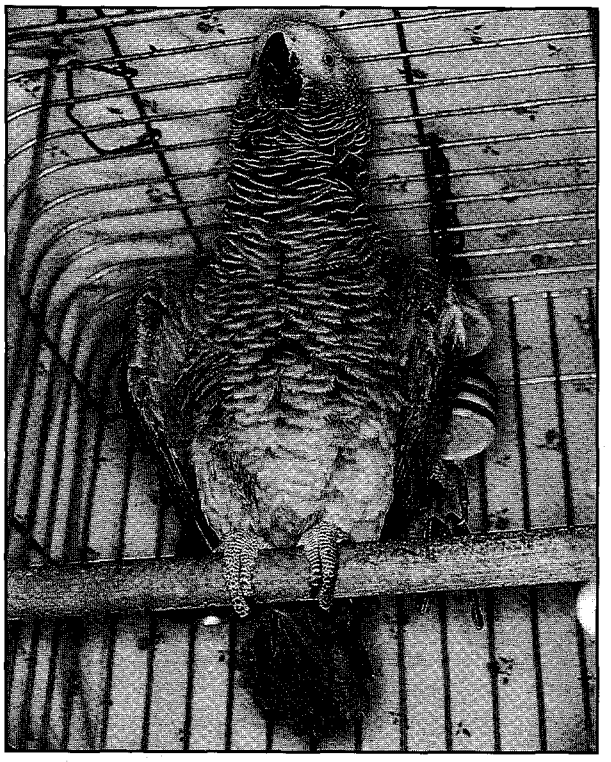

Figure 16.4: *African grey parrot showing wing fluttering associated with hypocalcaemic tetany.*

ing a rapid response. Long term treatment is aimed at correcting the diet and calcium-vitamin D_3 supplementation, such as ACE-High (Vetark®).

Vitamin E deficiencies

Birds so affected are seen with varying degrees of paralysis, and respond to selenium and vitamin E supplementation (Harrison and Harrison 1986).

In older birds, vitamin E deficiencies are characterised by CNS signs, in particular ataxia and torticollis (Coles 1985; Lowenstine 1986; Lawton 1988a). The underlying lesion is ischaemic necrosis with neuronal degeneration, demyelination, and pronounced oedema (Lowenstine 1986). Classical muscular dystrophy or white muscle disease also occurs in young birds.

Vitamin B deficiencies

Dietary problems in young birds result in incoordination, ataxia or so called "star gazing" in chicks, and are especially associated with the lack of thiamine. Fish eating water birds also may develop a thiamine deficiency and show CNS signs similar to cerebrocortical necrosis in sheep (Humphreys 1985).

Table 16.4: Causes of possible neurological problems in birds.

Ataxia	Arthritis Botulism Egg Binding Hypocalcaemic tetany Lead poisoning Nutritional osteodystrophy Paramyxovirus Trauma Vitamin B deficiency Vitamin E deficiency
Paresis	Abdominal masses Egg binding Excercise restriction Gonadal tumours Lead poisoning Nutritional osteodystrophy Paramyxovirus Renal tumours Selenium deficiencies Trauma Vitamin E deficiency
Seizures	Botulism Dehydration Hypocalcaemic tetany Lead poisoning Selenium deficiencies Toxicity Trauma Vitamin B deficiency

Abdominal masses

Paresis and lameness in any bird may be associated with an abdominal mass, usually a gonadal or kidney tumour (Cooper and Lawton 1988). The neurological signs may be directly caused by the increased pressure on the sciatic nerve plexus causing an inability to perch (Blackmore and Cooper 1982; Reece 1987), or indirectly due to the altered centre of gravity resulting from the abdominal mass (Cooper and Lawton 1988) (Figure 16.5).

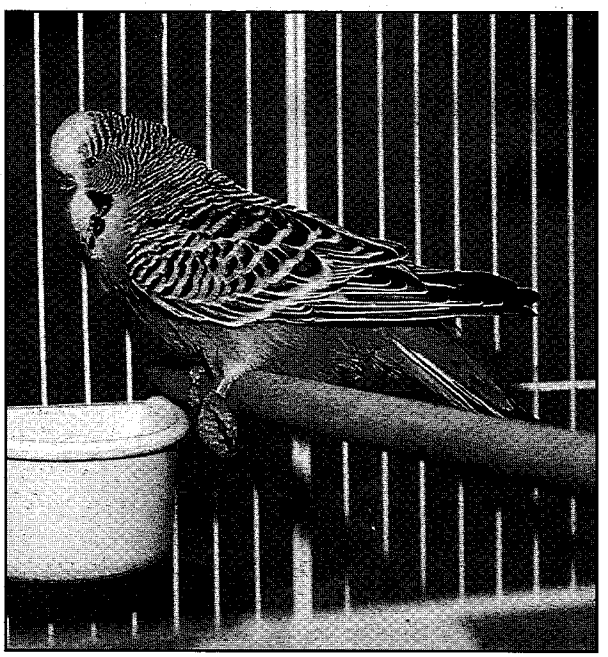

Figure 16.5: Budgerigar with paresis due to an abdominal mass.

Toxicity

Birds, like reptiles, are very sensitive to certain drugs and chemicals. Metronidazole can cause convulsions, which may be seen in birds treated for mouth canker or Trichomonasis. Dimetridazole has been shown to cause neurological signs in budgerigars, because of neuronal necrosis (Lancaster and Hooper 1991).

Organophosphorus poisoning can occur as a result of the use of the dichlorvos for treating external parasites. This is especially a problem in insectivorous birds, which eat insects already poisoned by the insecticide.

Botulism - water fowl are very prone to botulism toxicity. Developing maggots concentrate the toxin in their body tissues and are immune to its effects, but the level of toxin can prove lethal to the ducks that feed on such maggots (Barry 1986).

The clinical signs include weakness and ataxia which may progress to total flaccid paralysis, but may be acute in onset, and death in ducklings may occur in 15 minutes. Treatment with botulism antitoxin may be effective (Barry 1986).

Lead poisoning has been reported in water birds (Humphreys 1985) and psittacine birds (McDonald 1986). In water birds it usually results from ingestion of lead weights cast aside by anglers, or from lead gun shot. In psittacines, the lead poisoning may result from a wider range of sources, such as chewing lead on stained glass windows, old cages, or even discarded champagne tops.

Clinical signs appear several days after exposure to the source of the lead, but once the signs develop the course may be rapid and result in death. The severity of the disease is dependent upon the amount of lead ingested, the period of exposure and the size of the particles.

Lead encephalopathies result from diffuse perivascular oedema, increased cerebrospinal fluid production, and necrosis of neurones throughout the CNS (Smith *et al* 1972). Lead may also act directly at the neuronal level by affecting metabolism. Muscular weakness, which commonly accompanies poisoning with lead, is though to be the direct effect of demyelination (McDonald 1986).

Clinical signs are vague and include lethargy, weakness, ataxia, torticollis, blindness, circling or convulsions. McDonald (1986) sites two key features as haemoglobinuria and CNS signs. Radiography may be helpful but is not diagnostic as there are other causes or radio-opaque foreign bodies in birds. Blood lead concentrations must be estimated to give a definitive diagnosis, but often the presenting clinical signs and the dramatic response to treatment allows one to make a retrospective diagnosis.

Treatment is with calcium EDTA, 35-40 mg/kg BID for five days, which binds with the lead to form a water soluble non-toxic complex capable of being excreted. Response to treatment is dramatic. Mildly affected birds become free of signs within 48-72 hours. The more severe the CNS signs seen prior to treatment, the poorer is the prognosis. If seizures are present, control is attempted with diazepam at a dose rate of 0.5-1 mg/kg intramuscularly tid.

Paramyxovirus infections

Infection by these viruses may lead to neurological signs, the best known virus causing Newcastle disease. This virus affects most species of birds (Clubb 1983; 1986; Ashton 1988; Leach *et al* 1988). It has been isolated from over 100 species of birds, 35 of which are parrots (Luthgen 1981). There are 9 serologically distinct avian paramyxoviruses, and Newcastle disease is identified as Paramyxovirus 1 (PMV-1) (Ashton 1988).

In most birds there are no pathognomonic lesions or clinical signs seen. PMV-1 and PMV-3 may cause neurological signs in psittacines (Leach *et al* 1988). However, any neurological signs seen in pigeons, especially wing droop or torticollis, should suggest a Paramyxovirus infection until it can be ruled out (see

Figure 16.6). The clinical signs may include incoordination, head shaking, tremors or nodding, torticollis, and paralysis. Ataxia and neurological signs may persist in birds that recover from the infection. Diagnosis is by the isolation and culture of the virus, by demonstration of the haemaglutinating virus, or fluorescent antibody tests.

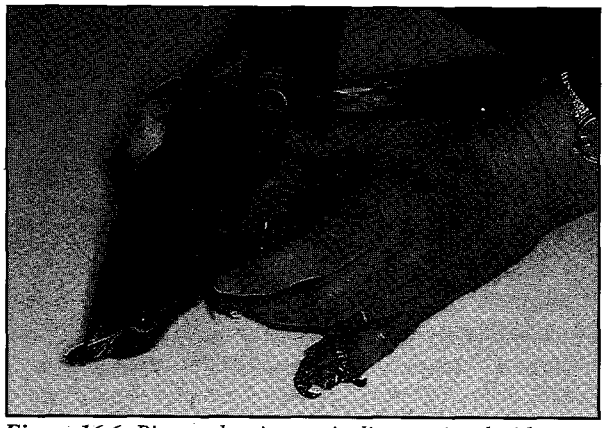

Figure 16.6: *Pigeon showing torticolis associated with Paramyxovirus infection.*

Trauma

Avulsion of the brachial plexus has been described in 5 birds as a cause of wing paralysis and muscle atrophy, and should be considered in any road traffic injured bird (Smiley *et al* 1988). However, it should be noted that it may be difficult to assess the degree of damage because of the behaviour of these wild birds and the lack of responses to noxious stimulants even on the normal wing.

Behavioural Problems

These may be seen in birds (Lawton 1988b). Neurosis, which in its early stages may not be very noticeable, is seen as agitation, such as hopping from perch to perch, or a continual shaking of the head in a figure eight pattern or a continuing dipping of the head from side to side (Dilger and Bell 1982). It is possible that this may be misdiagnosed as a neurological problem.

ECTOTHERMS

REPTILES

The reptilian spinal cord is different from mammals in that it extends to the tail tip (Davies 1981). Unlike mammals, the spinal cord retains a considerable amount of autonomy from the brain, as it possesses locomotor control centres (Davies 1981). A more detailed description of neurological disease in reptiles is given in Lawton (1992).

SNAKES

Neurological signs seen in snakes are generally associated with a loss of righting reflex, convulsions, inability to constrict, inability to strike at their prey with resulting cachexia, or lack of muscle tone.

The righting reflex of the snake is easily assessed by turning the snake on to its back, in the same way of testing that of a mammal (see Figure 16.7). Ataxia and incoordination of the snake is demonstrated by holding the snake by the mid body with head down, and seeing whether or not it is able to raise up in a straight line without jerking or twisting to an unnatural position. Muscle tone is assessed by its ability to grip when draped around an arm, as it is the natural instinct for any snake, once looped around an object, to start constricting in order to hang on. Defects of the neurological system may well cause problems with any of these responses.

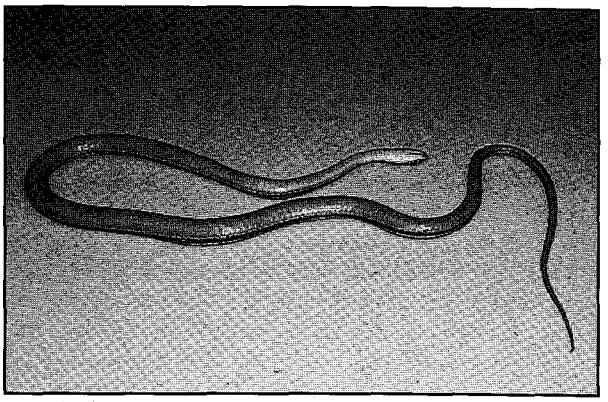

Figure 16.7: *Garter Snake showing loss of righting reflex associated with thiamine deficiency.*

Convulsions

Convulsions, twitching or coma are commonly seen in snakes (Cooper and Jackson 1981; Marcus 1981; Lawrence 1985a). The differential diagnosis includes dietary problems, septicaemia, colic, poisoning, dehydration, electrolyte imbalance (hypoglycaemia), as well as spinal cord damage. Convulsions associated with terminal septicaemia are most commonly associated with respiratory disease.

Fractures

Fracture of the spine, usually traumatic (Frye 1981) can result in a flaccid paralysis distal to the fracture site, a distended cloaca, and reduction or lack of response to stimuli, such as a needle prick or pressure (Cooper and Jackson 1981) (Figure 16.8).

Diagnosis is by radiography. The prognosis is more favourable then the same injury seen in mammals. With diuretics, corticosteroids and conservative therapy, such as force feeding, there is a reasonable prognosis (Russo 1985a). Usually, external casts are used; it is possible to use a plastic piping or tubing to stabilise the fracture site (Frye 1981; Peavy 1977).

Thiamine Deficiency

Snakes are fed on whole prey, therefore dietary problems are uncommon other than in fish eating snakes,

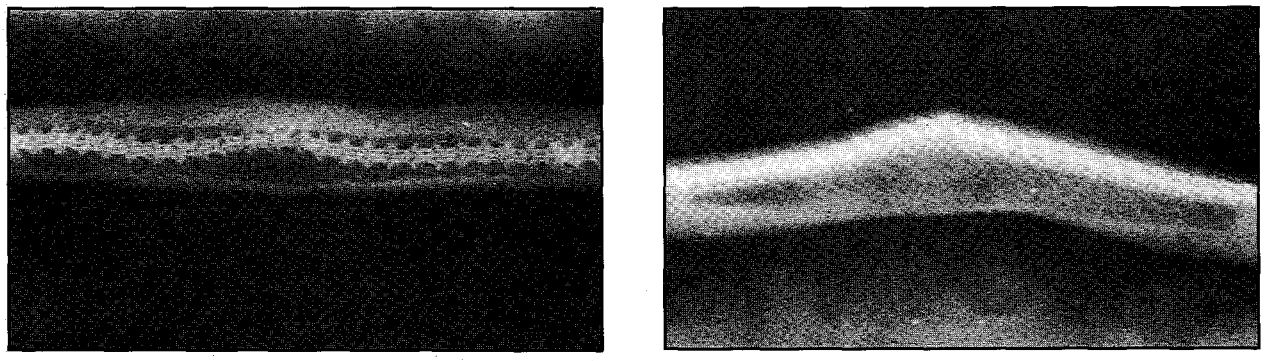

Figure 16.8: Garter snake with a fractured spine.

such as garter and dice snakes. These snakes, in captivity, tend to be fed on a variety of frozen white fish. Freezing not only decreases the amount of vitamins readily available to the snake, but also, in certain types of fish, increases the amount of thiaminase activity, which can result in a lack of available vitamin B_1 (Frye 1979; Lawrence 1985a). The presenting clinical signs are convulsions, incoordination, torticollis, or inability to strike correctly at its prey.

Recovering in response to thiamine at 25 mg/kg is dramatic. Prevention of future problems is by providing a more suitable diet, reducing the thiaminase activity, or by the addition of thiamine to the diet. Methods include heating the fish in boiling water for 60 seconds in order to deproteinize the thiaminase, and additional supplementation by placing thiamine directly onto the fish. Garter snakes are easily encouraged to eat earthworms, pinkies (baby mice), or even

Table 16.5: Causes of possible neurological problems in reptiles.

Ataxia	Abscessation Antibiotics (certain types) Fractures Freeze damage (Tortoises) Hypocalcaemia Hypothermia Thiamine deficiency (Snakes & Crocodilians) Toxicity Vitamin B deficiency (lizards)
Paresis	Abscessation Boid inclusion body disease (Snakes) Egg binding Fractures Freeze damage (Tortoises) Nutritional secondary osteodystrophy Trauma Vitamin B deficiency (lizards)
Seizures	Antibiotics (certain types) Boid inclusion body disease (Snakes) Colic (Snakes) Dehydration Electrolyte imbalance Hypocalcaemia Hypoglycaemia (Snakes & Crocodilians) Liver disease Paramyxovirus infection (Snakes) Renal failure Septicaemia (Lizards & Snakes) Thiamine deficiency (Snakes & Crocodilians) Toxicity

cat food which do not result in problems. If at first they are not too keen, gently smearing the new food with white bait will attract the snake.

Toxicity

Convulsions in snakes may be associated with organophosphorus poisoning, for example, as a result of the use of dichlorvos for the treatment of external parasites. This is particularly prevalent if the snake is fed while in the presence of the dichlorvos strip (Vapona, ICI). Treatment is supportive; partially cooling the snake will reduce the severity of the convulsions and reduce the risk of damage, and injection with atropine is also recommended. Any remaining dichlorvos must be removed from the tank.

Certain other drugs, particularly antibiotics, can be toxic to reptiles, resulting in incoordination or convulsions. These antibiotics include metronidazole, gentamicin, canamycin, neomycin, streptomycin, and polymyxin B (Jackson 1976; Holt 1981; Marcus 1981; Lawrence 1985a). The aminoglycosides are particularly toxic when used in conjunction with anaesthetics, because of their action of neuromuscular blockade.

Other substances which may affect the snake include iodine tincture, iodoform, lime, sulphur, nicotine salts (including nicotine from smokers' fingers), naphthalene, paraffin, ether, chloroform, alcohol, paint solvents, lactic base, and wood preservatives (Lawrence 1985a).

LIZARDS

Like most exotics, inadequate diets and supplementation are responsible for the majority of neurological problems.

Calcium: phosphorus: vitamin D_3 imbalance

A lizard fed an insectivorous, or vegetarian diet, which is low in calcium but high in phosphorus will develop nutritional osteodystrophy. The most common presenting sign in an affected lizard is neurological deficits (Redisch 1977; Russo 1985b; Fowler 1986). Lack of calcium can result in hypocalcaemic tetany, seen as a bilateral or unilateral twitching of the muscles or paraplegia. True osteodystrophy can be presented as a lameness, either because of the presence of a "pathological" fracture, or mechanical interference to locomotion by the inflammatory changes of the surrounding tissues (Lawrence 1985b) (see Figure 16.9 & 16.10). In the case of hypocalcaemic tetany, response to intravenous calcium is dramatic.

Nutritional osteodystrophy is treated by dietary supplementation, increasing calcium and vitamin D_3. The use of a baby food such as Millupa® (fruit or vegetable types) force fed with the supplement to the lizard is the method of choice, as the lizards have a soft jaw which causes problems when they try to eat more solid food.

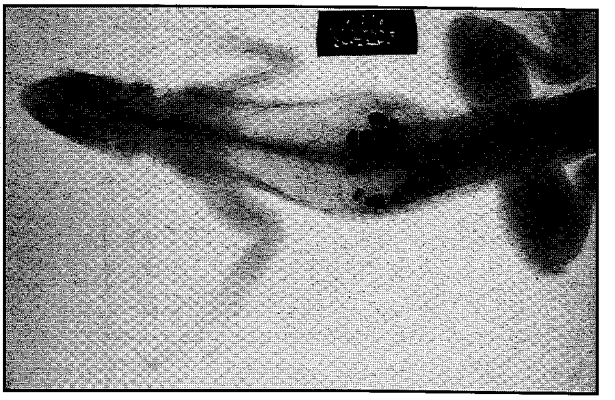

Figure 16.9: Sever osteodystrophy in an iguana, there is substantial reaction around the femurs (osteodystrophia fibrosa). The gravel in the intestines is often found in osteodystrophic lizards.

Fractures

Any lame lizard with a swelling in one of its limbs should be radiographed to rule out "pathological" fractures, and if necessary a blood sample for calcium concentration and a calcium:phosphorus ratio is also recommended (Figure 16.10). Treatment of secondary

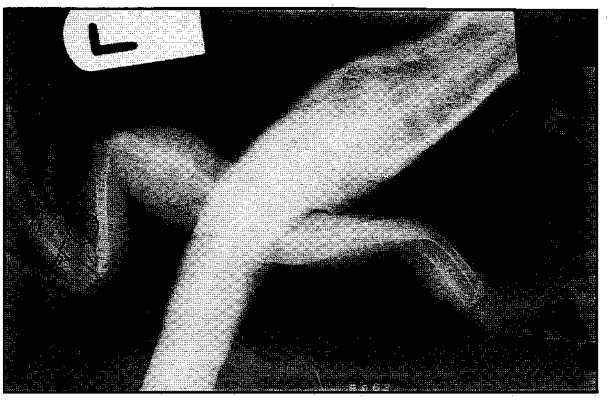

Figure 16.10: "Pathological" fracture of the femur of an iguana associated with nutritional secondary osteodystrophy.

"pathological" fractures of the limbs alone should be by external fixation, such as a light-weight cast made from Hexalite® (Millpledge), plaster of Paris, modified splints or dressings (Redisch 1977; Frye 1981).

Fractured spines, either simple or compression fractures, are usually traumatic and associated with osteodystrophy (Frye 1981). The prognosis is always guarded, but nursing and confinement may result in improvement.

Vitamin B deficiencies

Other nutritional problems are associated with the B vitamin complex deficiencies. Biotin deficiency may be seen, particularly in monitor lizards fed raw eggs (Frye 1979). The clinical signs are general muscle weakness, and diagnosis is based on the response to supplementation with vitamin B complexes, especially biotin. Lawrence (1985b) advises the use of B vitamin complex routinely, when no other cause for paresis can be found.

TORTOISES

Neurological problems in tortoises include unilateral or bilateral paresis, circling, inability to hold the head up, or over-extension of the head, together with inability to feed properly.

Egg binding

Hind limb paralysis should always be investigated by radiography. Occasionally it may be due to trauma to the limb itself, or to the carapace (dorsal part of the shell), and resulting damage to the spinal cord, as in injuries caused by lawn mowers commonly seen affecting American box tortoises.

However, hind limb paresis or paralysis is associated more usually with pressure in the abdomen caused by egg binding, and is diagnosed on a whole body radiograph. Such a tortoise may show excess wearing on claws of the hind limb and sometimes on the plastron, where they have been digging to lay their eggs. Others may show only anorexia, and an inability or unwillingness to move.

Treatment is by injection with calcium 0.5 ml/kg IM for up to two days, increasing the ambient temperature, and bathing. Subsequently, oxytocin up to a maximum of 6 IU is given, continuing with the increased temperature and baths. If this is not successful in removing the number of eggs that have been counted on the radiograph, this procedure may be repeated after a days rest. If this still is not successful, coeliotomy and salpingotomy are indicated.

Freeze damage

A tortoise walking around in circles may have neurological damage associated with a freezing episode sustained during hibernation. Such signs also may be caused by toxaemia. Damage to the CNS often results in the head being held over to one side. Such a tortoise may keep its head to one side permanently and walk in circles. This condition similarly is seen in tortoises with hepatopathy caused by gout or micro abscesses affecting the liver. Treatment is supportive, but the prognosis is guarded.

In the case of brain damage, diagnostic tests are of limited value, although there may be differences in the pupillary light reflex, but they are not reliable (Cooper and Jackson 1981). Reduced sensitivity to stimuli may be detectable, or conversely there may be lower threshold as a result of which the reptile exhibits excitability or hypersensitivity. Administration of thiamine to all cases may be useful.

Blindness in the tortoise frequently is noted after freezing episodes and may be associated with hyphaema, unilateral or bilateral vitreal haze, unilateral or bilateral lenticular opacities, or true retinal damage. The retinal damage is noted on ophthalmoscopic examination as a general lack of reflectivity and of the normal structure of the retina, which instead of being the normal bright red, green, and brown, tends to be a dull grey with a lack of the cellular structure. Tortoises may show various signs associated with these freezing episodes, partly dependent on the changes that have occurred to their eyes and all may be presented as neurological problems. A blind tortoise will not feed itself and is reluctant to move about.

The retinal damage does respond well to supplementation with high doses of vitamin A but it may take anything up to 18 months for the sight to return. Even mild lenticular opacities may disappear with supportive therapy over a long period of time. In the meantime, it is essential that tortoises be hand fed until they are able to eat. Such tortoises, even without examining the eyes with an ophthalmoscope, should be suspected of being blind by their lack of a menace response. On assessing the "Jackson ratio" they are found to be on or above the mean line, thus distinguishing from post hibernation anorexia.

Over-extension of the head backwards, lack of movement or gasping is often associated with septicaemia or respiratory problems and, again, these may be diagnosed or ruled out by radiography.

Fractures limbs occasionally are found in tortoises and are treated easily by replacing the limb into the shell and by use of epoxy resin to immobilise it within the shell for a period of 3 months, which generally results in healing.

CROCODILES

Osteodystrophy and thiamine deficiencies may cause neurological signs similar to those already described (Jubb 1992) and show some response within 24 hours to 30 mg thiamine injections.

Hypoglycaemia has been reported as a cause of neurological problems in crocodiles (Wallach 1971; Frye 1986). This is a stress-induced hypoglycaemia, which results in muscle tremors, loss of righting reflex, mydriasis, and reduction of the metabolic rate. Treatment is with glucose, given orally, at 3 gm/kg and the removal of the stressful conditions (Frye 1986).

FISH

Neurological problems in fish are associated generally with an inability of the fish to swim, or an abnormality of posture or buoyancy.

Buoyancy

Buoyancy is affected if the fish is floating upside down at the surface, or sinking to the bottom unable to support itself. Lack of buoyancy is often associated with failure of the swim bladder to function, which may be related to primary or secondary bacterial sep-

ticaemia (Collins 1980). If caused by secondary bacterial septicaemia, this is usually in the terminal phase. In goldfish, it is often a primary problem of unknown aetiology and with no signs of generalised disease (Collins 1980). Affected fish may still live a normal life and feed, provided they are not unduly stressed.

Balance

The balance of fish is disturbed when the fish is seen tilting over to one side, usually related to an encephalitis (Collins 1980).

Flashing

When the fish swims from side to side in an erratic or jerky motion, the result is that the shiny scales of the ventrum glint in the light, a phenomenon known as "flashing". The type of swimming may be considered a neurological problem by the owner, but is probably due to external parasites, with the fish swimming and scraping against the bottom of the rocks in an attempt to rid itself of the external burden. Some fish may be seen to demonstrate erratic movements or spurts of activity and some may even jump out of the water. Treatment is by control of the causative parasite.

INVERTEBRATES

Invertebrates are very sensitive to chemical agents, especially insecticides, which may cause muscle spasms, incoordination, and finally death. There is no specific treatment for toxicity other than to remove the invertebrates from the source of the insecticide and keep it in a well ventilated cage. Limbs may also be damaged or amputated due to incorrect handling or inappropriate furniture in their terrarium, but they will often regenerate (Cooper 1991).

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Acronyms and Abbreviations

5HT	5-hydroxytriptamine (Serotonin)
ACTH	Adrenocorticotrophic hormone
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
ANA	Antinuclear antibody
AST	Aspartate aminotransferase
BAEP	Brainstem auditory evoked potential
BID	Twice daily
BSP	Bromsulphalein
Ca	Caudal
CDRM	Chronic degenerative radiculomyelopathy (Degenerative myelopathy)
CEMAP	Compound evoked muscle action potential
CHP	Coonhound paralysis
CIN	Cerebral ischaemic necrosis (Feline ischaemic encephalopathy)
CK	Creatine kinase
CMG	Cystometrogram
CN	Cranial nerve
CNS	Central nervous system
CSF	Cerebrospinal fluid
CT	Computed tomography
DV	Dorsoventral
ECG	Electrocardiogram
EEG	Electroencephalogram
EMG	Electromyography
FCE	Fibrocartilaginous embolism
FELV	Feline leukaemia virus
FIE	Feline ischaemic encephalopathy
FIP	Feline infectious peritonitis
FIV	Feline immunodeficiency virus
FPL	Feline panleukopenia
FPL	Functional profile length
GABA	Gamma-aminobutyric acid
GAN	Giant axonal neuropathy
GME	Granulomatous meningoencephalomyelitis
ICP	Intracranial pressure
IM	Intramuscular
IU	International units
IV	Intravenous
LAT	Lateral
LDH	Lactate dehydrogenase
LM	Lateromedial
LMN	Lower motor neuron
LMO	Lateromedial oblique
MRI	Magnetic resonance imaging
MUCP	Maximum urethral closure pressure
MUP	Maximal urethral pressure
MP	Motor unit potential
NCV	Nerve conduction velocity
OP	Organophosphorus
PCV	Packed cell volume (Haematocrit)
PL	Pelvic Limb
PO	Per os
QID	Four times daily
RF	Radiofrequency
SARD	Sudden acquired retinal degeneration syndrome
SC	Subcutaneous
SID	Once daily
T1	Longitudinal relaxation time in MRI
T2	Transverse relaxation time in MRI
TID	Three times daily
TL	Thoracic limb
TRH	Thyrotropin releasing hormone
TSH	Thyroid stimulating hormone
UMN	Upper motor neuron
UPP	Urethral pressure profile
UTI	Urinary tract infection
VD	Ventrodorsal

Index

Appendix

Breed-related Neurological Disorders

BREED	AGE	DISORDER
Abyssinian cat	Juvenile	Myasthenia gravis
Afghan hound	Juvenile	Hereditary myelopathy
	Juvenile	Narcolepsy
Airedale terrier	Juvenile	Cerebellar malformation
	Juvenile	Narcolepsy
Akita	Juvenile	Deafness
Australian shepherd	Juvenile	Deafness
Basset hound	Juvenile	Cervical vertebral malformation
	Adult	Intervertebral disc disease
Beagle	Juvenile	Narcolepsy
	Juvenile	Globoid cell leukodystrophy
	Juvenile	Cerebellar degeneration
	Juvenile	Breed associated meningitis
	Adult	Idiopathic epilepsy
	Adult	Intervertebral disc disease
Belgian tervueren	Juvenile/Adult	Idiopathic epilepsy
Bernese mountain dog	Juvenile	Hypomyelinogenesis
	Juvenile	Breed associated meningitis
Bichon frise	Juvenile	Shaker disease
Border collie	Juvenile	Cerebellar degeneration
	Juvenile	Deafness
	Juvenile	Sensory neuropathy
Borzoi	Juvenile	Cervical spondylomyelopathy
Boston terrier	Juvenile	Hydrocephalus
	Juvenile	Deafness
	Juvenile	Vertebral abnormalities
	Adult	Primary brain tumours
Bouvier des Flandres	Juvenile	Laryngeal paralysis
Boxer	Juvenile	Progressive axonopathy
	Adult	Primary brain tumours
Brittany spaniel	Juvenile	Spinal muscular atrophy
	Juvenile	Cerebellar degeneration
Bull mastiff	Juvenile	Cerebellar degeneration
Bull terrier	Juvenile	Deafness
Burmese cat	Juvenile	Deafness
	Juvenile	Congenital vestibular disease
Cairn terrier	Juvenile	Globoid cell leukodystrophy
Cavalier King Charles spaniel	Juvenile	Collapsing syndrome
	Adult	Intervertebral disc disease
Chihuahua	Juvenile	Hydrocephalus
	Juvenile	Atlantoaxial subluxation
	Adult	Intervertebral disc disease
Chow chow	Juvenile	Myotonia
	Juvenile	Cerebellar hypoplasia
	Juvenile	Hypomyelinogenesis
Clumber spaniel	Juvenile	Mitochondrial myopathy
Cocker spaniel	Juvenile	Deafness
	Juvenile/Adult	Idiopathic epilepsy
	Adult	Idiopathic facial paralysis
	Adult	Intervertebral disc disease

Corgi	Adult	Intervertebral disc disease
Dachshund	Juvenile	Sensory neuropathy
	Juvenile	Narcolepsy
	Juvenile	Deafness
	Juvenile	Ceroid lipofuscinosis
	Adult	Intervertebral disc disease
Dalmatian	Juvenile	Cavitating leukodystrophy
	Juvenile	Deafness
Doberman	Juvenile	Deafness
	Juvenile	Congenital vestibular disease
	Juvenile	Narcolepsy
	Adult	Dancing Doberman disease
	Adult	Sensory neuronopathy
	Adult	Cervical spondylomyelopathy
English bulldog	Juvenile	Spina bifida
	Juvenile	Hemivertebra
English pointer	Juvenile	Sensory (mutilating) neuropathy
English setter	Juvenile	Deafness
	Adult	Ceroid lipofuscinosis
Fox terrier	Juvenile	Deafness
	Juvenile	Congenital vestibular disease
	Juvenile	Congenital myasthenia gravis
	Juvenile	Hereditary ataxia
German shepherd dog	Juvenile	Congenital vestibular disease
	Juvenile	Deafness
	Juvenile	Glycogenosis
	Juvenile	Spinal neuroepithelioma
	Adult	Giant axonal neuropathy
	Juvenile/Adult	Idiopathic epilepsy
	Adult	Degenerative myelopathy
	Adult	Lumbosacral disease
	Adult	Masticatory myositis
Golden retriever	Juvenile	Muscular dystrophy
	Juvenile/Adult	Idiopathic epilepsy
Great Dane	Juvenile	Cervical spondylomyelopathy
	Juvenile	Central core myopathy
	Adult	Distal polyneuropathy
Greyhound	Adult	Exertional myopathy
Irish setter	Juvenile	Cerebellar malformation
	Juvenile	Megaoesophagus
	Juvenile	Narcolepsy
	Juvenile/Adult	Idiopathic epilepsy
	Adult	Laryngeal paralysis
Irish wolfhound	Juvenile	Cervical spondylomyelopathy
Jack Russell terrier	Juvenile	Congenital myasthenia gravis
	Juvenile	Hereditary ataxia
Keeshond	Juvenile/Adult	Idiopathic epilepsy
Kerry blue terrier	Juvenile	Cerebellar degeneration
Labrador retriever	Juvenile	Narcolepsy
	Juvenile	Hereditary myopathy
	Juvenile	Cerebellar degeneration
	Juvenile	Distal polyneuropathy
	Juvenile/adult	Idiopathic epilepsy
Lhasa apso	Juvenile	Hydrocephalus
	Adult	Intervertebral disc disease
Maltese terrier	Juvenile	Shaker dog disease
	Juvenile	Hydrocephalus
Manx cat	Juvenile	Sacrocaudal dysgenesis

Miniature poodle	Juvenile	Atlantoaxial subluxation
	Juvenile	Narcolepsy
	Adult	Intervertebral disc disease
	Adult	Idiopathic epilepsy
Miniature schnauzer	Adult	Idiopathic epilepsy
Old English sheepdog	Juvenile	Deafness
Pekinese	Juvenile	Intervertebral disc disease
	Juvenile	Atlantoaxial subluxation
	Juvenile	Vertebral anomalies
Persian cat	Juvenile	Mannosidosis
Pomeranian	Juvenile	Hydrocephalus
Pug	Juvenile	Hemivertebra
	Adult	Encephalitis
Rhodesian ridgeback	Juvenile	Meningocoele
	Juvenile	Deafness
Rough collie	Juvenile	Deafness
	Adult	Degenerative myelopathy
Rottweiler	Juvenile	Neuroaxonal dystrophy
	Adult	Leukoencephalomyelopathy
	Adult	Distal polyneuropathy
St Bernard	Juvenile	Narcolepsy
	Adult	Idiopathic epilepsy
Scottish terrier	Juvenile	Scotty cramp
Sheltie	Juvenile	Dermatomyositis
Shih tzu	Juvenile	Atlantoaxial subluxation
	Adult	Intervertebral disc disease
Siamese cat	Juvenile	Gangliosidosis
	Juvenile	Mucopolysaccharidosis
	Juvenile	Idiopathic vestibular disease
	Juvenile	Deafness
Siberian husky	Juvenile	Laryngeal paralysis
	Adult	Degenerative myelopathy
Springer spaniel	Juvenile	Congenital myasthenia gravis
	Adult	Intervertebral disc disease
	Adult	Fucosidosis
Staffordshire terrier	Juvenile	Myotonia
Tibetan mastiff	Juvenile	Hypertrophic neuropathy
Weimaraner	Juvenile	Syringomyelia
	Juvenile	Hypomyelination
West Highland white terrier	Juvenile	Globoid cell leukodystrophy
Yorkshire terrier	Juvenile	Atlantoaxial subluxation
	Juvenile	Hydrocephalus
	Adult	Intervertebral disc disease